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BASAL METABOLIC RATES IN SOME OF THE PSYCHONEUROSES*

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ONE hundred cases which were referred to the laboratory for basal metabolic rate determinations were classified and studied. Each case exhibited two or more of the cardinal signs of hyperthyroidism, described by Moebius and by Charcot, and the degree of manifestation of the symptoms was well pronounced. Since the patients were sent to this hospital for admitted reasons of nervousness, the basal metabolic rate determinations were resorted to in the attempt to determine, if possible, whether the primary affliction was of a purely nervous or of an hyperthyroid nature.

It cannot be stated with any degree of finality, however, even in the evidence of the most reliable basal metabolic determinations, whether the cause of the symptoms is central, autonomic, or whether it is of an endocrine origin. Even a hasty review of the literature on basal metabolism in its application to the diagnosis of or differentiation between goiter affection and certain, so-called, functional nervous manifestations, exposes a tangle of views, which at first seems almost hopeless. Thus, Means and Aub[1] conclude that basal metabolic determinations differentiate between true thyroidism and simple neurasthenia, and make possible early diagnosis of exophthalmic goiter.

Boothby[2] categorically states that "for practical diagnosis, an increased basal metabolic rate indicates hyperthyroidism, either from exophthalmic goiter or thyroid adenoma, provided active acromegaly is ruled out and the group of febrile diseases is eliminated by a normal temperature curve." He states further that "the basal metabolic rate is of the utmost value in the differential diagnosis of mild hyperthyroidism (of either type) and a neurosis

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simulating hyperthyroidism which often may be associated with an enlarged colloid goiter or a thyroid adenoma which is not producing an excess of the thyroid hormone * * * An increased metabolic rate in a neurotic patient—he believes—is due to the fact that the rate was not obtained with the patient under basal or standard conditions."

In another paper the same author[3] states that "in the differential diagnosis of adenoma with hyperthyroidism and exophthalmic goiter it is obviously necessary to exclude definitely cases presenting the syndrome of neurasthenia, usually of the cardiac type, with many of the earmarks of hyperthyroidism, but in which no hyperthyroidism or overactivity of the thyroid is usually present." In further emphasizing his belief in the sufficiency of the basal metabolic rate determination in establishing or substantiating a diagnosis, this author states that "patients having simply neurasthenia, even those whose symptoms most closely simulate hyperthyroidism, do not have persistently elevated basal metabolic rates." In this article he again states emphatically that in his opinion "a normal basal metabolic rate eliminates hyperthyroidism." In another article[4] the same author again states that "basal metabolic rate serves as an accurate diagnostic aid in the recognition of the presence or absence of hyperthyroidism." Sandiford[5] believes as does Boothby, and states that "the basal metabolic rate is of greatest value in thyroid disorders because it gives *a very accurate, mathematical index* (the italics are the writer's) of the degree of functional activity of the thyroid gland. * * * No definite instance of an increased basal metabolic rate has been found in that group of cases known as neurasthenia or chronic nervous exhaustion. The basal metabolic rate has proved, therefore, to be of great value in the differential diagnosis of neurosis simulating hyperthyroidism, and true hyperthyroidism." McGuire[6] believes that a patient with hyperthyroidism may have a high metabolic rate and not be as seriously ill as another having a lower rate but whose structural changes in the heart, kidney, and liver are rather pronounced. This is in seeming contradiction with the above cited opinion of Sandiford. He believes, however, that the onset of hyperthyroidism is insidious and difficult to recognize in its early stages, when the metabolic rate clearly differentiates it from hysteria, neurasthenia, and other conditions with which it may be confused.

Woodbury[7] comes to the conclusion that thyrotoxic psychosis does not exist as a distinct entity, but that commonly designated neurotic or psychotic symptoms arise in thyrotoxic cases. These can be separated from psychoneurotic states free from endocrine involvements by determining their basal metabolic rate. Miller and Raulston[8] frequently observed patients in whom the diagnosis of neurasthenia has been made, but in whom manifestations similar to those observed in hyperthyroidism were present. In the light of Cannon's experimental observations, they conclude that in this type of patients there is continually present in the blood an increased thyroid secretion, and that on excitement or moderate exertion this secretion further increases to an extent sufficient to bring forth definite symptoms of hyperthyroidism. Therefore, for purposes of study, they feel justified in consider-

ing as a possible hyperthyroidism every case in which the chief complaint is nervousness.

It is believed by those holding the above cited views that the degree of the so-called hyperthyroidism and, hence, the height of the metabolic rate accompanying it, is proportional to the degree of the secretory activity of the thyroid gland. In this connection Kessel and his collaborators[9] make the following statements: "The potency of the thyroid hormone is proportional to its iodine content. In the hyperplastic gland of the exophthalmic goiter there is a diminution of iodine. There is no direct proof that an increased thyroid secretion is present in hyperplasia. What data are available indicate a decreased output and storage." And as for elevation of basal metabolism, they believe that it may occur in other conditions dissociated from goiter or alterations in the involuntary nervous system. In another paper the same authors,[10] after a study of 86 cases possessing the classic symptomatology of exophthalmic goiter, come to the conclusive opinion that it is unwise to designate the condition of exophthalmic goiter as an endocrine disorder, and they, therefore, propose the abolition of such terms as "hyperthyroidism" and "dysthyroidism." Their experience had impressed them with the fact that the majority of patients presenting exophthalmic goiter give a history past or present of autonomic imbalance. Since the causative relation between autonomic imbalance and exophthalmic goiter has not been established, they do not commit themselves, but think it improbable for thyroid hyperplasia to be the cause of the imbalance.

Brooks[11] likewise believes that preexisting emotional states are the primary causes of the conditions frequently designated as Graves' disease. If the condition is a transient one, he calls it, "Physiological hyperthyroidism" and thinks it "is brought about by an abnormally great demand on the thyroid as the result of developmental growth associated with too much emotional output. When these factors are either diminished within the normal limits or directed into other channels, automatically the overaction of the gland, together with other secondary factors that may be associated with it, drop toward the normal; but if the urge is too long continued, or if fixed habits of demand and response be established, the condition will develop either into Graves' disease or take on a neurasthenic phase likely to ruin the life of the individual. It appears, then, to be but a normal response to an exaggerated or abnormal demand with the final establishment of a tissue habit." These statements of Brooks are based upon long continued and careful observation, and although lacking the backing and convincing reasoning of carefully planned experimentation, embody in them views which may be considered as strong probabilities.

More perplexing to the clinician, who seeks for an unequivocal significance in the basal metabolic values, is the view of Carlson[12] who speaks of "apparent reliable clinical reports to the effect that the, so-called, hyperthyroidism or toxic goiter may be present with a normal metabolic rate and that hyperthyroidism or myxedema may be present and parallel with a high or normal basal metabolism. * * * Mere increase in the size of the gland,

mere hyperplasia does not mean more gland activity or more secretion. Thyroid hyperplasia and thyroid adenoma occur without physiologic disturbances, although the size, structure and the chemistry of the thyroid seem to be identical with those in the toxic goiter." He, too, believes that the primary relation of exophthalmic goiter to the thyroid gland has not been definitely established.

An interesting and instructive contradiction is afforded by the following two papers in which "hysteria" appears to be the central factor. Juarros[13] speaks of the frequency with which diagnosis confuses hysteria and hyperthyroidism in women. He thinks this is due to an equivocal conception of hysteria. To avoid such confusion he looks for symptoms of hyperthyroidism in all women with manifestations simulating hysteria, but in whom the so-called hysterical mentality (?) is lacking. (The interrogation mark is the writer's.) In other words, he believes that *the hysterical manifestations are caused by the existing hyperthyroidism.* How erroneous this may be is shown by an experience of Danna[14] who reports a case of a boy with a so-called well defined *psychoneurosis, hysterical type,* which was entirely relieved of the neurotic symptoms *through the administration of thyroid treatment.* Aub, who as previously cited, believed in 1919 the basal metabolic rate determinations to be a safe means for the recognition of exophthalmic goiter, later[15] expressed the opinion that the regulation of metabolism is also under the control of many factors independent of the internal glands, and, hence, of the thyroid.

Timme[16] has well summarized the situation, and the writer takes the liberty of citing considerable of his statement. He says: "The endocrine system has no constant quantities, only variables which need a higher type of mathematics, a calculus which furnishes information about differentials, but the end result has to be integrated by integral calculus. * * * The answer to any integral calculus problem dealing with variables is never one term or absolute quantity. It is always represented in a series of terms combined in a formula of functions of the factors involved. To illustrate: A middle-aged woman gives the clinical aspects of myxedema; her basal metabolic rate was determined by three investigations made by two investigators and varied from +80.0 per cent to +100.0 per cent. Hence, the man who saw her refused to believe it was myxedema, and refused to give her thyroid. Examining the case further, we found that she had intense headache, and roentgenographic examination showed she had an enlarged sella turcica and a bitemporal hemianapsia with a diminution in vision. Therefore, it was a case of hypophysial mass, plus myxedema.

She was given thyroid. Within two or three days she began to improve; her headaches began to diminish, and the basal metabolic rate became lower, on no other treatment than the administration of the thyroid. It does not mean that the deficiency of the thyroid produced a high metabolic rate; the high rate may be due to the pressure on parts of the brain. In any event, it means that the integration of the syndrome is a formula, and that is what we have to consider in all the innumerable problems which con-

front us, and the formula is one which involves all the varying activities of the glandular elements."

Regardless as to whether the study of the metabolic values of these cases will point towards an increased, normal, or low rate in any of the ordinarily designated nervous afflictions here classified, in the light of the above review of the opinions on the subjects of hyperthyroidism, neuroses, and metabolism, we feel justified in saying, *a priori*, that it will add nothing definite to the determination of the causes of these afflictions. Nervous manifestations forming the syndromes according to which the cases studied in this paper have been classified, like metabolism, are mere symptoms, and, by all probability, are not called forth by the same cause or combination of causes. We come to realize more and more that in the realms of the psychoses and psychoneuroses as much confusion prevails at present as in the general field of endocrinology. Hence, in the following study we aim to point out the extent of increased or decreased basal metabolism and the frequency of their occurrence in the neuroses groups under investigation.

The method used in the determination of the metabolic rate was the same as was described by the writer[17] in a previous publication. It may be appropriate to remark at this point that emotional states, even when sufficiently concealed or suppressed, have a great effect upon the metabolic rate of all subjects, and especially of those afflicted with psychoneurotic instabilities. Such patients may be at perfect physical rest during the test period, and yet yield a metabolic rate of from +10.0 per cent to +50.0 per cent above their true basal metabolic rate. Occasionally an emotional state will result in a reduced rate, but this happens very seldom. The factors causing such an emotional state may be: a fleeting stimulating thought of a pleasant or unpleasant nature; a sexual stimulation due to the presence of a person who directly or through association stimulates the patient; the personality of the technician; the fear of the patient that the test will disclose to the physician that which he is carefully trying to conceal; and many others.

Such increase in metabolism, however, is not due to the thyroid secretion, since the effects of the stimulation are registered almost instantaneously. It is well established now that the response of metabolism to thyroid secretion is considerably delayed, and is quite gradual as regards both, the increase and decrease in its intensity, as was shown by Plummer and Boothby.[18] On the other hand, an increase in the secretion of the suprarenal glands causes a rapid and marked increase in the metabolic rate, which declines almost as rapidly. Boothby and Sandiford[19] showed that adrenalin not only caused an invariable increase in the heat production of their test subjects, but that it also occasioned an increase in the ventilation and in the respiratory quotient. We found in our neurotic patients, who showed a higher metabolic rate than their true basal, on a repeat test, that there was a change in the rate of their ventilation and in the respiratory quotient, and we conclude from this that the high metabolic rate was due not to the thyroid overaction, but to the stimulation of the suprarenals.

In any event, the above discussion indicates, from a technical point of

view, that in determining basal metabolic rates on neurotic patients the following points must be carefully observed: (1) that it be done by a competent person who understands neurotic patients and who is more or less familiar with their individual histories and who knows how to gain their confidence, (2) that more than one test be made previous to forming final judgment and (3) that an apparatus which reliably registers the ventilation rate and the respiratory quotient be used in preference to any other make.

For purposes of uniformity and for more universal understanding of the results, the rates obtained in our study were recorded in terms of plus and minus percentile variation from a known "standard of comparison." This standard was 39.5 calories per square meter of body surface area per hour, and is the Aub and DuBois standard of normal rate for males between the ages of 20 and 40 years. It was used in this study as the "standard of comparison" because none of our patients exceeded the age of 40.

The expression "standard of comparison" is here used in preference to the expression "normal standard," as an indication of the probability of the adopted "normal standard" not being sufficiently reliable. In a personal conversation with the writer, Dr. W. M. Boothby has expressed the opinion that the DuBois standard may not be regarded as a finality in its adequacy and should be supplemented by additional determinations in the thousands, if possible. Even then, the question as to whether a "standard" so selected represents a "normal" condition remains an open one. It is possible that the case in this instance is similar to the case of the "normal gastric acidity." It has been shown by Rhefuss, Hawk, and their collaborators[20] that there are normally high gastric acidities. This was corroborated by the writer[21] who pointed out that there are also normally low gastric acidities and that the degrees of the acidities are not to be regarded as the factors of importance, since they may vary considerably in the same individual, but that the constancy of the so-called "percentile relationship of the titrable factors" may prove to be the determining factor of normality. Something similar may be true with regard to basal metabolic rates. Indeed, in another paper we shall show that this view has a high degree of probability.

In the numerical order, the cases here reported were as follows: Hysteria, 42; Neurasthenia, 25; Anxiety, 16; Organic, 8; Constitutional phychopathic states, 4; Traumatic neurosis, 3; Alcoholics, 2. Summaries of the rates of each of the groups are given in the corresponding tables following.

As seen from Table I, 42 cases with a primary diagnosis of hysteria were tested with a total of 96 basal metabolic determinations. Of the group as a whole, three determinations did not vary from the standard of comparison, and were, therefore, denoted as ±0.0 per cent; thirty-two determinations had a percentile variation between ±0.0 per cent and +5.0 per cent ten determinations had a percentile variation between +5.0 per cent and +10.0 per cent; the rate of fifteen determinations exceeded +10.0 per cent. Seventeen determinations had a variation between ±0.0 per cent and –5.0 per cent; twelve determinations possessed a variation between –5.0 per cent and

–10.0 per cent; eleven determinations were below –10.0 per cent. In terms of cases, twenty-four, or 57.0 per cent had an average rate variation between ±0.0 per cent and +10.0 per cent; nine cases, or 21.0 per cent possessed a rate variation between ±0.0 per cent and –10.0 per cent, making a total of 78.0 per cent of cases of this group possessing a rate lying within the ±10.0 per cent limits.

TABLE I—THE GROUP OF HYSTERIAS

NO.	NAME	BASAL	METABOLIC	RATES EXPRESSED IN PERCENTILE VARIATION	
1	N. J. H.	+ 5.0%	+ 2.5%		
2	R. C.	– 2.5	– 0.2		
3	G. S.	+11.1	– 1.0	+ 1.5	
4	C. M.	– 1.5	– 6.6		
5	V. A. B.	+ 2.0	– 6.0	± 0.0	– 9.3
6	F. B.	– 9.6	– 8.6	–27.3	–30.0
7	W. B.	+11.6	+14.6		
8	W. DeC.	– 5.0	– 5.0		
9	M. O. C.	+ 3.6	+ 7.3		
10	A. R. C.	– 9.6	– 9.6	– 6.3	–13.0
11	H. G. D.	+ 1.8	+ 1.8		
12	R. J. D.	+ 1.7	+ 0.5		
13	F. A. D.	+ 4.0	+ 7.0		
14	H. J. D.	– 1.5	– 2.3		
15	E. B.	+ 4.8	+ 1.3		
16	W. H.	+ 3.8	+ 3.8	+ 3.8	
17	F. H.	+ 5.0	+ 4.6		
18	H. J.	+ 3.5	+ 3.5	– 1.3	– 3.5
19	R. J.	+ 8.6	+10.8		
20	H. T. J.	+ 1.3	+ 1.5		
21	X. K.	– 0.3	– 3.0		
22	A. L.	– 1.5	+ 3.5		
23	P. O. M.	–26.3	–24.8		
24	E. M.	+15.2	+15.7		
25	X. R.	– 5.0			
26	Ras.	+ 5.5	+ 4.3		
27	H. R.	+14.0	+14.0		
28	H. S.	+ 8.0	+10.9		
29	Spr.	+11.4	+13.2		
30	Gos.	– 6.5	– 3.1	– 6.3	– 8.0
31	E. W. T.	+ 2.3			
32	A. S.	+ 1.2	– 0.9		
33	W. R.	+ 9.2			
34	J. E.	+12.3	+11.3	+13.0	+13.4
35	G. A.	+ 8.9	± 0.0		
36	H. S.	+ 5.5			
37	Mu.	+32.9	+36.7		
38	M. O.	± 0.0	– 0.5	+ 6.8	
39	L. R. B.	+ 3.5	+ 1.0		
40	T. B.	+ 0.1	+ 0.8		
41	D. D.	–41.0	–50.0	– 7.3	
42	W. W.	+ 8.8	+ 1.5		

Six cases, or 15.0 per cent possessed a rate variation exceeding +10.0 per cent, and three cases, or 7.0 per cent possessed rates with a variation below –10.0 per cent, making a total of 22.0 per cent of cases of this group which, according to the prevailing standard, would be regarded as out of the normal range. Considering that all the cases of this group showed a number of the cardinal signs of disturbed metabolism, and that they were sent to the laboratory as suspicious cases, the percentage of those having

rates which might be regarded as either excessive or insufficient is surprisingly low.

Classifying the cases of this group into subgroups, according to the amends in the diagnoses, it was found that nineteen cases were diagnosed as pure hysteria; of these eleven, or 60.0 per cent possessed rates not exceeding +10.0 per cent; five cases, or 26.0 per cent possessed rates lying between ±0.0 per cent and –10.0 per cent, making a total of 86.0 per cent of cases exhibiting metabolic rates which are not regarded at present as either too high or too low. Three cases, or 14.0 per cent possessed rates exceeding +10.0 per cent, and none fell below –10.0 per cent. Hence, the percentages of the average, high, and low rates in this subgroup are practically the same as the percentages of the group as a whole.

The next subgroup was found to consist of six cases in which endocrine involvements, chiefly of the thyroid type, have been definitely added to the primary diagnosis of hysteria. The vagueness of the statements of the secondary diagnoses in these cases and the metabolic rates are worthy of note. They were as follows:

1. Hysteria with hyperthyroidism, with metabolic rates of –1.5 per cent, and –2.3 per cent.
2. Hysteria with toxic goiter, with metabolic rates of –0.3 per cent, and –3.0 per cent.
3. Hysteria with endocrine imbalance, with metabolic rates of +8.0 per cent; and +10.9 per cent.
4. Hysteria with dysthyreosis, with a metabolic rate of +2.3 per cent.
5. Hysteria with endocrinopathy, with a metabolic rate of +9.2 per cent.
6. Hysteria with endocrine imbalance, with metabolic rates of +8.9 per cent and ±0.0 per cent.

It is perhaps of significance that none of these cases possessed rates above +10.0 per cent, whereas in the pure hysteria cases occurred with rates as high as +35.0 per cent. However, the average values of this subgroup, each case of which exhibited the cardinal signs of Basedows' disease to such an extent that the gland involvement was definitely indicated in the diagnosis, were practically the same as the averages of the subgroup of simple hysterias. Thus, the average of the plus values of the simple hysterias was +6.65 per cent, and of the hysterias with suspected endocrine disturbance +6.7 per cent. The average of the minus values of the pure hysterias was –3.8 per cent, and of the hysterias with the endocrine status under suspicion was –1.8 per cent. The total average of the pure hysterias was +3.7 per cent, and that of the hysterias with the endocrine status under definite suspicion was +3.2 per cent.

Of the subgroup of five cases diagnosed as hysteria with the admixture of anxiety expressions, two cases possessed rates exceeding +10.0 per cent, the rate of one was below –10.0 per cent, the rate of the two others were within the ±10.0 per cent limits. It may seem from these data as though the presence of the disturbance which results in manifestations conveniently designated as anxiety, is paralleled by higher metabolic rates, but as will be

shown under the discussion of the group of anxiety cases, this is only seemingly so, and is probably due to the small number of cases under consideration.

Three cases were diagnosed as hysteria with psychopathic manifestations, all of which possessed basal metabolic rates not exceeding +10.0 per cent. Two cases were diagnosed as hysteria on the basis of mental deficiency, one of which did not exceed +10.0 per cent, while the other had a rate considerably below –10.0 per cent. Two cases were diagnosed as hysteria with hypochondriacal tendencies, the rates of both were within the ±10.0 per cent limits. Two cases were diagnosed as hysteria with bradycardia; of these one had an average rate of –16.4 per cent, the other had an average rate of +12.3 per cent. One case was diagnosed as hysteria with neurasthenic admixtures, one as hysteria with alcoholic tendencies, and one as hysteria on the basis of hermaphroditism. The first possessed rates not exceeding +10.0 per cent, the average rate of the last one was of a minus sign, but not below –10.0 per cent. It may be seen from this outline that of all the subgroups discussed, the one of the simple hysterias indicates a more frequent occurrence of cases with rates lying out of the ±10.0 per cent limits, and that the coexistence, with the factors causing hysteria, of other disturbances leading to the apparent necessity of so-called secondary diagnoses, has no effect upon the basal metabolic rates.

THE NEURASTHENIAS

Twenty-five cases were diagnosed as neurasthenias, and their rates were as shown in Table II.

As may be seen from Table II, the total of the rate determinations was 64. Of the group as a whole, two determinations equaled ±0.0 per cent; ten determinations had a percentile variation not exceeding +5.0 per cent; thirteen had a percentile variation not over +10.0 per cent and thirteen exceeded +10.0 per cent. Five determinations had a percentile variation between ±0.0 per cent and –5.0 per cent; fourteen between –5.0 per cent and –10.0 per cent, and two were below –10.0 per cent. In terms of cases, 10, or 40.0 per cent had an average percentile variation not exceeding +10.0 per cent; eight cases, or 32.0 per cent had percentile variations not lower than –10.0 per cent; making a total of 72.0 per cent of cases of this group possessing rates which are considered according to the present standards as neither too high nor too low. Six cases, or 24.0 per cent, possessed rates with a percentile variation exceeding +10.0 per cent, and one case, or 4.0 per cent, possessed a rate with a percentile variation below –10.0 per cent, thus making a total of 28.0 per cent of the cases of this group which according to the present adopted standard would be regarded as out of the normal range.

Comparing these percentages with those of the group of the hysterias, it is seen that they are almost identical in their totalities, (78.0 per cent as compared with 72.0 per cent of cases with rates within the ±10.0 per cent limits, and 22.0 per cent as compared with 28.0 per cent of cases without the ±10.0 per cent limits) and considering that in this group, as in the group of hysterias, the cases showed pronouncedly the cardinal signs of disturbed

metabolism and that some of them were previously established as "high raters," the percentages may be regarded likewise as surprisingly low. Since neurasthenias more generally than hysterias have been confused with cases of thyroid or metabolic disorders, in the plus direction, it might be supposed that the average rates of the neurasthenics, especially of those lying without the adopted high normal limit would be greater than those of the hysterias. This, however, does not prove to be the case. Thus, the average percentile rate variation of the hysterics whose rates exceeded +10.0 per cent was 16.4 per cent, and that of the corresponding cases among the neurasthenics was 17.7 per cent.

TABLE II

NO.	NAME	BASAL	METABOLIC	RATES EXPRESSED IN PERCENTILE VARIATION	
43	McM.	– 4.1%	– 2.9%	– 8.3	
44	R. L. S.	– 4.8	– 6.0		
45	W. S.	– 6.1	– 6.0		
46	G. S.	– 7.3	– 7.6		
47	V.	– 5.6	– 3.5		
49	W. T. H.	+ 5.8	+ 3.0		
48	B.	+24.0			
50	R. C.	– 5.4	± 0.0		
51	C. D.	+ 5.0	+11.7	+12.6	+14.4
52	G. R. F.	+ 0.3	+ 3.4	+ 3.4	– 3.0
53	G. B. G.	– 6.6	–12.6	–11.4	
54	S.	+ 6.9	+ 6.9	+ 6.1	– 3.86
55	A. F.	+ 9.6	+ 8.0		
56	Th. M.	+ 9.0	+11.1	+12.7	
57	L. F.	+ 3.6	+ 6.6		
58	B. C.	+ 8.0	+ 6.6		
59	W. C.	+16.5			
60	F. W.	+17.5	+17.5	+18.5	+18.5
61	H. H. R.	+ 8.6	+ 7.8	+ 8.6	
62	T. D. C.	+ 2.5	± 0.0		
63	J. N.	– 1.0	+ 5.5		
64	D. R.	+40.5	+37.0		
65	C. R.	– 7.1	– 4.8	+ 2.3	+ 5.1
66	F. L.	+ 6.6	+ 3.6		
67	A. C.	– 8.5	– 8.5	– 6.7	– 7.0

Classifying the cases of this group into subgroups according to their amended diagnoses, it was found that six cases were diagnosed as pure or simple neurasthenias. Of these, four cases, or 80.0 per cent, possessed basal metabolic rates with percentile variations between –3.0 per cent and –9.0 per cent, one case possessed a basal average rate of +4.4 per cent and none were without the limits of +10.0 per cent. The average of the plus values of this group was +4.4 per cent, that of the minus values –5.62 per cent, and the total average was –3.95 per cent. These figures are rather interesting as compared with the figures of the corresponding group of the hysterias and point to a lower metabolic rate among the so-called simple neurasthenias than among the simple hysterias.

Eight cases were diagnosed as neurasthenia with endocrine involvements of the thyroid type. They were as follows:

1. Neurasthenia with thyroidectomy residuals, with B. M. Rates +24.0 per cent.

2. Neurasthenia with mild dysthyreosis, with B. M. Rates –5.4 per cent, and ±0.0 per cent.

3. Neurasthenia with mild hyperthyroidism, with B. M. Rates +5.0 per cent, +11.0 per cent, +12.6 per cent, +14.4 per cent.

4. Neurasthenia with pronounced tachycardia and with hyperthyroidism strongly suspected, with B. M. Rates +0.3 per cent, +3.4 per cent, +3.4 per cent, –3.0 per cent.

5. Neurasthenia with hysterical admixtures and with endocrine disturbance, with B. M. Rates –6.6 per cent, –12.6 per cent, –11.4 per cent.

6. Neurasthenia secondary to hyperthyroidism, with B. M. Rates +6.9 per cent, +6.9 per cent, +6.1 per cent, –3.8 per cent.

7. Neurasthenia with hyperthyroidism under suspicion, with B. M. Rates of +9.6 per cent, +8.0 per cent.

8. Neurasthenia with probable dysthyreosis, with B. M. Rates +9.0 per cent, +11.1 per cent, +12.7 per cent.

It is thus seen that three cases, or 37.5 per cent of this group had a metabolic percentile variation exceeding +10.0 per cent, whereas none of the cases of the corresponding subgroup of the hysterias exceeded this rate. This points to the probability of "high metabolic raters" occurring more frequently among neurasthenics suspected of having metabolic disturbances, than among the corresponding hysterics, although as stated above, the average metabolic rates of the groups are nearly the same. The one case possessing a metabolic rate with a percentile variation below –10.0 per cent was a special case and will be discussed elsewhere.

Two cases were diagnosed as neurasthenia with psychasthenic admixtures, one of which also had marked homosexual tendencies. The latter will likewise be discussed in greater detail in a following paper. Their metabolic rates were for the first +16.5 per cent, and for the second +17.5 per cent, +17.5 per cent, +18.5 per cent, and +18.5 per cent. One case was diagnosed as neurasthenia with gastrointestinal toxicosis and had rates of +40.0 per cent, and +37.0 per cent. The remaining cases were all within the ±10.0 per cent limits, indicating that such concomitants as mental subnormality, renal dysfunction, tuberculosis, progressive muscular atrophy, have no effect upon the basal metabolic rate of the cases studied in this group, provided their temperature curve is normal.

THE GROUP OF ANXIETIES

There were sixteen cases with a primary diagnosis of anxiety, as shown in Table III.

Eight of the cases were diagnosed as pure anxiety, the rest having concomitants or admixtures such as mitral regurgitation, chronic nephritis, hysterical and psychasthenic manifestations, mild myocarditis, etc. One of the sixteen cases, diagnosed as pure anxiety, had a basal metabolic rate of +16.5 per cent and +15.7 per cent, and one, with valvular heart disease, possessed metabolic rates of +13.0 per cent and +13.8 per cent, making a total of 12.5 per cent of cases of this group with metabolic rates exceeding the +10.0

per cent limit. This is 2.5 per cent less than the percentage of the corresponding rates among the hysterics and 11.5 per cent less than the percentage of the same among the neurasthenics. The rates, too, are nearer the so-called border line.

The rates of the remaining cases of this group were within the ±10.0 per cent limits, indicating, as did the previous two groups, that admixtures or concomitants have no effect upon the rate of the basal metabolism of persons exhibiting the so-called anxiety syndrome.

TABLE III

NO.	NAME	BASAL	METABOLIC	RATES	EXPRESSED	IN	PERCENTILE	VARIATION
68	F. G. C.	− 4.0	± 0.0	+ 2.3	+6.3			
69	Hud.	− 0.8						
70	Sen.	− 2.8	+ 0.8					
71	M. H. L.	− 3.5	− 7.0					
72	W. K.	− 5.3	− 6.3	+ 5.3	+ 4.8			
73	A. K.	− 4.0	− 2.8					
74	F. A. G.	+10.1	+ 9.1					
75	M. E.	− 2.0	+ 2.3	+ 9.8	+ 8.0			
76	H. E.	+ 7.9	+ 5.6					
77	McC.	+16.5	+15.7					
78	E. E. A.	− 2.2	+ 1.5					
79	P. C.	+ 7.1	+ 4.6					
80	F. C.	+ 9.6						
81	A. F.	+ 5.0	+ 8.0					
82	Swn.	− 0.5	− 0.7	− 3.5	− 6.1			
83	F. S.	+13.0	+13.8					

The group of the constitutional psychopathic states consisted of four patients, all of the type commonly designated as inadequate personality. They were as follows:

No. 84. N. L. with a basal metabolic rate of +20.5%
No. 85. F. E. with a basal metabolic rate of + 1.5% and +5.5%
No. 86. C. H. C. with a basal metabolic rate of + 8.8% and −1.5%
No. 87. B. B. with a basal metabolic rate of + 6.8% and +8.4%

It is the writer's conviction that the rate of the first case was not basal, and that on repetition it would not exceed +10.0 per cent.

Three cases of traumatic neurosis possessed the following rates:

No. 88. R. J. C. with a basal metabolic rate of + 4.3%
No. 89. G. S. with a basal metabolic rate of + 0.5% and ±0.0%
No. 90. B. C. S. with a basal metabolic rate of + 4.0% and −0.7%

Reference could be made at this point to literature indicating that traumas of various types had definite effects upon the emotional states of the persons affected and causing the appearance of symptoms and even syndromes simulating those commonly recognized at present as due to hyperthyroidism or to exophthalmic goiter, and point out that none of our cases possessed rates of any magnitude deserving attention. However, since the literature reviewed on this subject by the writer dealt with the immediate effects of the traumatic injuries upon the general picture of the patient, and our rates were taken nearly four years after the injuries occurred, the discussion and the comparisons would prove valueless, or questionable in the least.

Two cases of alcoholism had the following rates:

No. 91. E. C. H. B. M. Rates −5.7%
No. 92. H. V. K. B. M. Rates +1.0%

A group of eight organic cases were subjected to basal metabolic rate measurements and are given below:

No. 93. J. H. Dysthyreosis, exophthalmic type with B. M. Rates of −0.5%, −0.9%, −0.5%
No. 94. H. S. Exophthalmic goiter, B. M. Rate −2.5%
No. 95. B. R. A. Hyperthyroidism, B. M. Rates −3.0%, +1.8%
No. 96. N. E. L. Tuberculosis, pulmonary, incipient, B. M. Rates +1.90%, −0.8%
No. 97. M. H. Bronchitis, chronic, B. M. Rates −5.8%, ±0.0%
No. 98. S. B. Neurosyphilis, B. M. Rates −8.0%, −6.1%
No. 99. O. S. Residuals, encephalitis epidemica, B. M. Rates +4.0%, +0.7%, −1.5%, −3.0%
No. 100. L. B. Exostoses, B. M. Rates +5.0%, ±1.2%

It is worthy to note that the three patients of this group which were diagnosed as primary thyroid cases with practically no outstanding symptoms recognizable by the psychiatrist as indicative of N-P involvements all had rates lying within the ±10.0 per cent limits, and that none had an average metabolic rate with a plus sign. The other cases necessitate no discussion.

SUMMARY AND DISCUSSION

One hundred of the cases admitted to this hospital during the previous two years were tested for their basal metabolic rates because of the presence of two or more of cardinal signs believed to be indicative of exophthalmic goiter. Only eight of the one hundred cases were found to be affected with primary organic afflictions, the remaining 92 being classified primarily as cases of a neuropsychiatric type. Of the group as a whole 15 cases, or only 15 per cent possessed rates with a percentile variation exceeding the +10.0 per cent limit, and only four cases, or 4.0 per cent possessed rates with a percentile variation below the −10.0 per cent limit, making a total of 19.0 per cent of cases with basal metabolic rates lying without the ±10.0 per cent limits. Kay[21] has examined one hundred cases belonging for the most part to the Great Lakes districts which were referred to him for basal metabolic rate determinations for the purpose of substantiating or disproving the temporary diagnosis of hyperthyroidism. He found that only about 33.0 per cent of his cases possessed rates exceeding the +10.0 per cent limit. Among our patients, most of whom likewise belong to the Great Lakes districts, only 15.0 per cent possessed rates exceeding the +10.0 per cent limit.

Further statistical study shows that the average of the plus rates of the group as a whole is +7.4 per cent, that of the minus rates −6.5 per cent, and the total average rate is +2.0 per cent. Less than 30.0 per cent of the cases studied by us had metabolic rates the average of which was qualitatively of a minus type. Less than one-third of these, or only about 10.0 per cent were below the −10.0 per cent limit. Bowman and Grabfield[22] studied fifty mental cases most of whom were insane, some suffered with epilepsy, cretinism, or myxedema. They found that 42 of their cases, or 84.0 per cent possessed basal metabolic rates with a minus sign, and expressed the opinion that the tendency towards a low basal metabolism in cases of mental disease is of

importance and merits consideration in formulating theories as to etiology and treatment. Our findings in connection with cases which may be designated as mild psychoneuroses differ radically from the findings of the above authors, and show that the group types of mental afflictions studied by Bowman and Grabfield and those studied by us affect the metabolic processes of the individuals in different directions.

The percentage of cases with rates exceeding the +10.0 per cent limit among the groups reviewed by us were as follows:

Hysterics	15.0%
Neurasthenics	24.0%
Anxieties	12.5%

indicating a more frequent occurrence of "high raters" among neurasthenics suspected of hyperthyroidism than among any of the other neuroses. The coexistence of secondary psychoneurotic manifestations or of organic concomitants of the types met with in our cases does not seem to influence the basal metabolic rate in any way.

The percentages of cases with metabolic rates below the –10.0 per cent limit were:

Hysterics	7.0%
Neurasthenics	4.0%
Anxieties	None

Our close observation of psychoneurotics with high metabolic rates has led us to the conclusion that the high rates in most instances are not due to an hyperthyroidism or exophthalmic goiter superimposed upon a well defined neurosis, but rather that the hyperthyroidism or the exophthalmic goiter are the direct consequences of or rather the necessary response to the mental state of the patients. Consequently any amount of surgical treatment such as ligation or even excision will only lead to an hypertrophy of the remaining tissue, frequently to such an extent as to make the postoperative basal metabolic function unstable and, in most instances, of a higher magnitude than it was previous to the operation. This seems to be especially true of "high raters" manifesting the anxiety syndrome complicated by some sexual complex. To perform any surgical operation, except the one absolutely warranted and found necessary after a joint consultation of an internist, surgeon, and a competent psychiatrist thoroughly acquainted with the case under consideration, means to introduce into the patient's life new points of fixation, added causes for fear and worry, and hence, an increased demand upon the thyroid, resulting, as stated above, in a basal metabolic rate exceeding the one before the operation. These are not mere speculative statements, but are statements of facts which will be brought out more clearly in a following publication.

Acknowledgment is here made to Dr. Chester L. Carlisle, Surgeon (R) in charge of this hospital, for his permission to prepare this paper, and to Miss F. L. Shuman, of our laboratory.

BIBLIOGRAPHY

[1]Means, J. H., and Aub, J. C.: The Basal Metabolism in Exophthalmic Goiter, Arch. Inter. Med., December, 1919, xxiv, 645-677.

[2]Boothby, W. M.: The Fundamental Classification of Disease by Basal Metabolic Rate, Jour. Am. Med. Assn., Jan. 8, 1921, lxxvi, 84-86.

[3]Boothby, W. M.: Adenoma of the Thyroid with Hyperthyroidism, etc., Endocrinology, Jan. 1921, v, No. 1, 1-20.

[4]Boothby, W. M.: The Basal Metabolic Rate in Hyperthyroidism Jour. Am. Med. Assn., July 23, 1922, lxxvii, No. 4, 252-255.

[5]Sandiford, I.: The Basal Metabolic Rate in Exophthalmic Goiter, Endocrinology, Jan.-March, 1920, iv, No. 1, 71-87.

[6]McGuire, S.: Metabolism as an Aid in Diagnosis, Prognosis, and Treatment of Hyperthyroidism, South Caro. Med. Assn. Jour., 1920, xvi, 107-119.

[7]Woodbury, M. S.: The Psychoneurotic Syndrome of Hyperthyroidism, Jour. Nerv. & Ment. Dis., 1918, xlvii, 401-410.

[8]Miller, J. L., and Raulston, B. O.: The Recognition of Mild Hyperthyroidism, Jour. Am. Med. Assn., Oct. 28, 1922, lxxix, No. 18, 1509-1511.

[9]Kessel, L., Lieb, C. C., and Hyman, H. T.: A Study of Exophthalmic Goiter and the Involuntary Nervous System, Jour. Am. Med. Assn., Sept. 30, 1922, lxxix, No. 14, 1216.

[10]Lieb, C. C., Hyman, H. T., and Kessel, L.: A Study of Exophthalmic Goiter and the Involuntary Nervous System, Jour. Am. Med. Assn., Sept. 30, 1922, lxxix, No. 14, 1099-1101.

[11]Brooks, H.: Physiological Hyperthyroidism, Endocrinology, 1921, v, No. 2, 177-189.

[12]Carlson, A. J.: Hypofunction and Hyperfunction of the Ductless Glands, Jour. Am. Med. Assn., July 8, 1922, lxxix, No. 2.

[13]Juarros, C.: Hyperthyroidism and Pseudohysteria, Plus Ultra, 1919, ii, 350-354, Through Endocrinology, Jan., 1921, v, No. 1.

[14]Dana, Chas.: The Somatic Causes of Psychoneuroses, Jour. Am. Med. Assn., 1920, lxxiv, 1139-1143.

[15]Aub, J. C.: The Relation of the Internal Secretion to Metabolism, Jour. Am. Med. Assn., July 8, 1922, lxxix, No. 2, 95-98.

[16]Timme, W.: Part of a Discussion, Jour. Am. Med. Assn., July 8, 1923, lxxix, No. 2, 107.

[17]Levine, B. S.: The Technic of Basal Metabolic Rate Determination in Psychoneurotic Patients, Jour. Lab. Clin. Med. Nov., 1922, viii, No. 2, 73-77.

[18]Plummer, H. S., and Boothby, W. M.: Specific Dynamic Action of Thyroxin., Am. Jour. Phys., March, 1921, iv, No. 2.

[19]Boothby, W. M., and Sandiford, I.: The Effect of Subcutaneous Injection of Adrenalin Chloride on the Heat Production, Blood Pressure, and Pulse Rate in Man. Am. Jour. Phys., Febr., 1920, li, No. 1.

[20]Rehfuss, M. E., and Hawk, P. B.: Gastric Analysis. I. Fundamental Principles, Jour. Am. Med. Assn., lxxvi, No. 6, 371-373.

[21]Levine, B. S.: Gastric Analysis and the Constancy of the Percentile Relationship Among the Titrable Factors of the Gastric Secretion, Jour. Lab. and Clin. Med., June, 1923, viii, No. 9, pp. 612-4.

[22]Kay, W. E.: A Study of One Hundred Cases Diagnosed as Hyperthyroidism, Jour. Am. Med. Assn., Dec. 23, 1922, lxxix, No. 26.

[23]Bowman, K. M., and Grabfield, G. P.: Basal Metabolism in Mental Disease, Archives of Neurology and Pschychiatry, March, 1923, ix, No. 3, 358-361.

CLINICAL AND LABORATORY PROCEDURES IN PEDIATRICS

By A. Levinson, M.D., Chicago, Ill.

(Continued from page 749.)

Roentgenography and Fluoroscopy in Children

THE roentgen ray is an important aid in both the diagnosis and treatment of many diseases of infants and children. It is, however, necessary to know what to ask for from the roentgenologist, and to be able to interpret the plate after it is developed, and above all to correlate the roentgenological and the clinical pictures. The problem of keeping the child quiet during examination can, in part be overcome by rapid work.

THE NORMAL CHEST

The roentgenogram of a normal chest is subject to wide variations, especially with reference to the bronchial marking, hilus shadow and nodes of calcifications. Indeed it is likely that a real normal chest seldom, if ever,

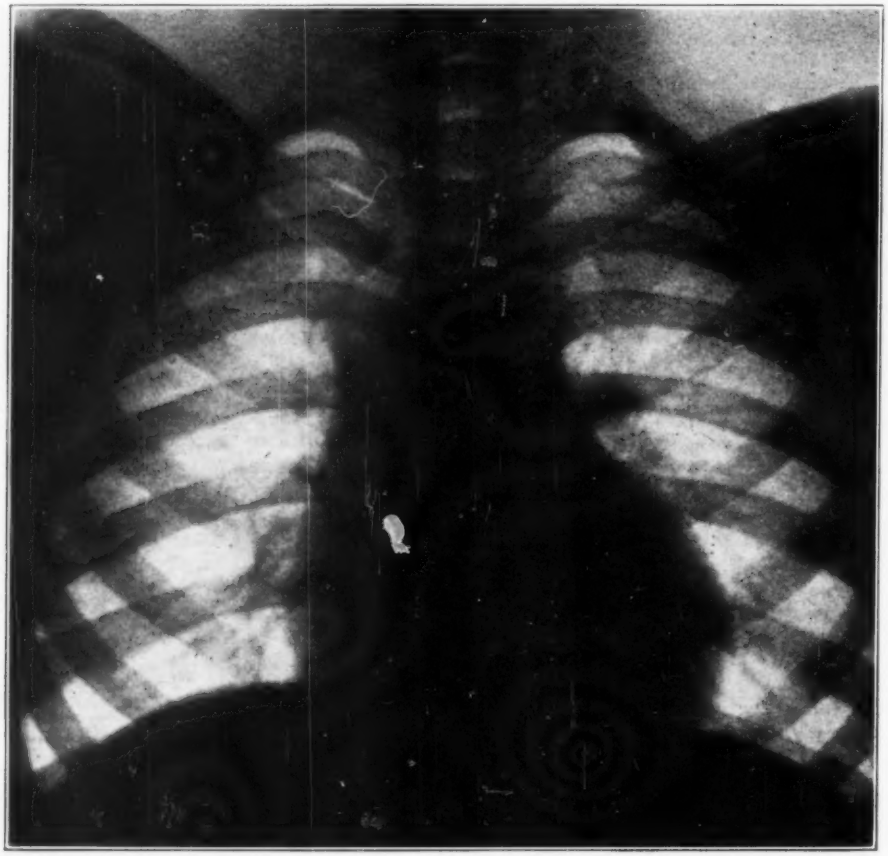

Fig. 32.—Chest of a child in good health showing some bronchial markings.

comes under observation, as any chest needing x-ray usually has some pathology in it to begin with. Furthermore, very few chests are clear of some infection or other. The term "normal" as generally used must therefore be considered as relative, rather than absolute.

A normal chest shows the outline of the heart, the lungs, the clavicle, the ribs, the diaphragm, and the scapula. An absolutely normal chest shows no areas of densities in the lungs. Some plates, however, show pronounced bronchial markings which fade before the outer third of the chest is reached. These children have usually gone through some previous lung infections

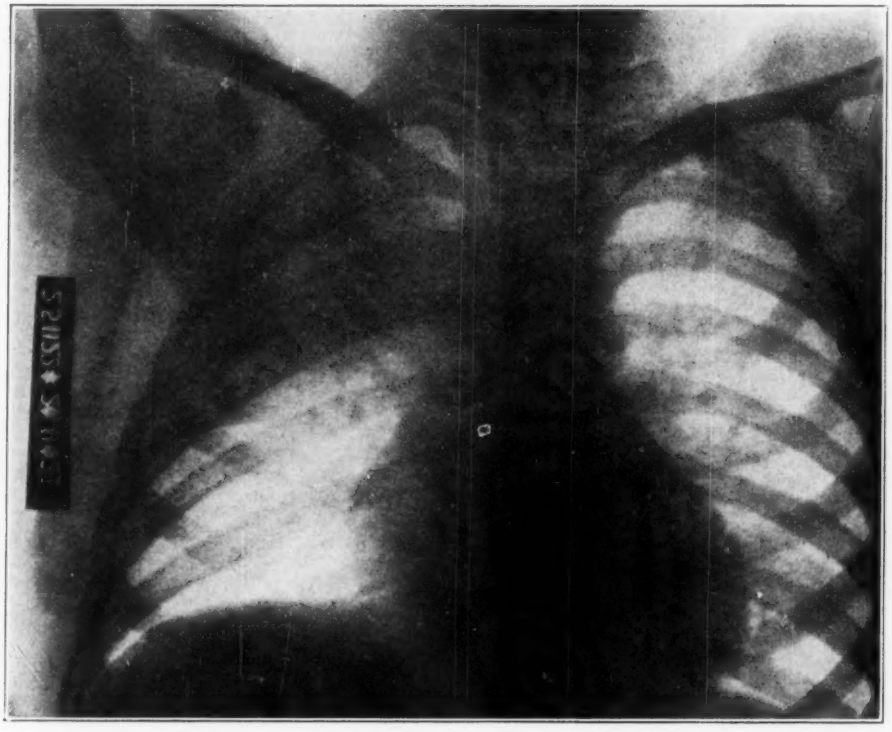

Fig. 33.—Lobor pneumonia. Consolidation of right upper lobe.

which left some bronchial markings (Fig. 32). No diagnosis of active pathology should therefore be made on these markings.

A hilus shadow, especially if it is subdivided into small areas, indicates an infection which may be tuberculous in character, but does not necessarily speak for an active infection, nor does it necessarily speak for a tuberculous process, as many other infections, especially influenza, may leave a hilus density. The same is true with calcified nodes. They are suggestive of a latent tuberculosis, but no diagnosis of this disease must be made merely on their presence.

DISEASES OF THE LUNGS AND PLEURA

Lobar pneumonia is characterized by a shadow of increased density of the lobe involved (Fig. 33). The structural markings are not seen as a rule.

The borderline between the consolidated and the unaffected portions of the lung is usually very sharp.

Bronchopneumonia may show only very little change in the plate. Both bronchitis and bronchopneumonia may show small areas of increased density along the bronchial tree variable in size and shape with rather indefinite outlines. These may occur anywhere, but are frequently found at the bases (Fig. 34).

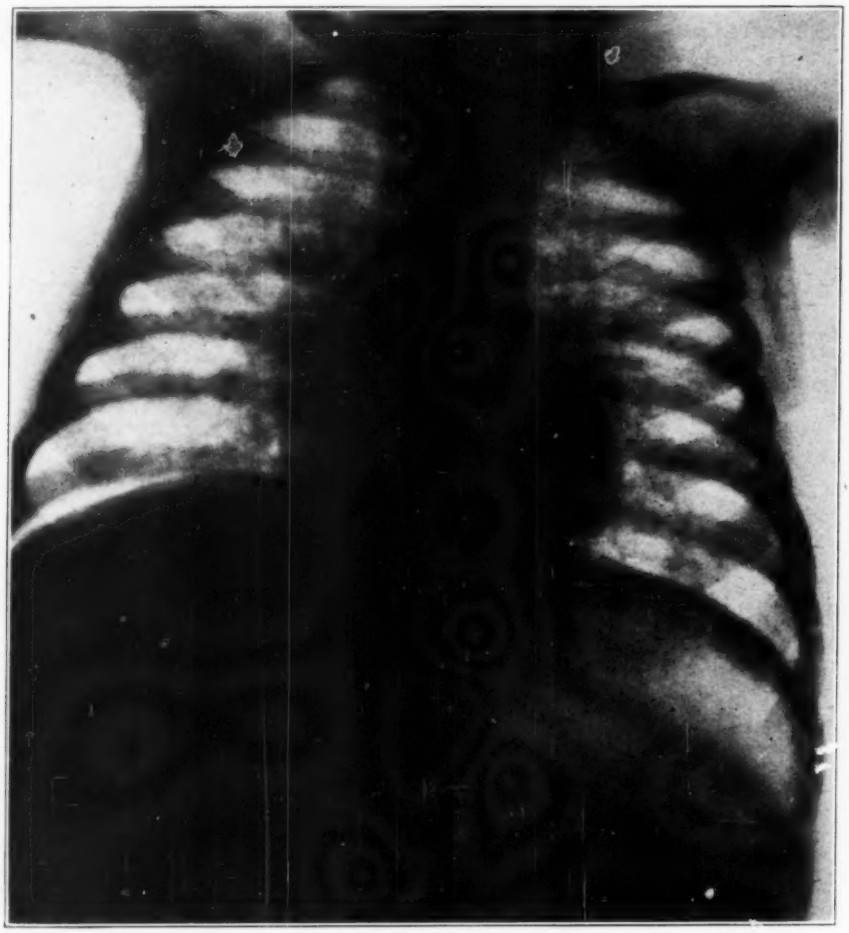

Fig. 34.—Bronchopneumonia.

Acute bronchitis may cause demonstrable roentgenographic changes. Chronic bronchitis may show increased markings followed well out into the periphery.

Tuberculous changes may be found anywhere in the lungs of children. The apical findings so frequently present in adults, however, are not common. Small shadows like a snowstorm scattered throughout the lungs are indicative of an acute miliary tuberculosis of the lungs (Fig. 35). The enlargement of the mediastinal shadow beyond the inner third of the chest speaks for enlarged tracheobronchial glands, which, in conjunction with

whispered bronchophony and positive tuberculin tests, speak for tuberculous glands, although no diagnosis of tuberculosis of tracheobronchial glands should be established on the hilus shadow.

Lung abscess is indicated by a clouding of the lung with a central necrotic area that is characterized by a dark area, of decreased resistance, surrounded by a dense peripheral zone.

Fluid in the chest cavity shows a shadow depending on the amount, on the location, and whether the fluid is free or encapsulated. Free fluid casts a shadow that may be seen to move upon change of position of the patient when viewed under the fluoroscope. It tends to seek a level. It may cause

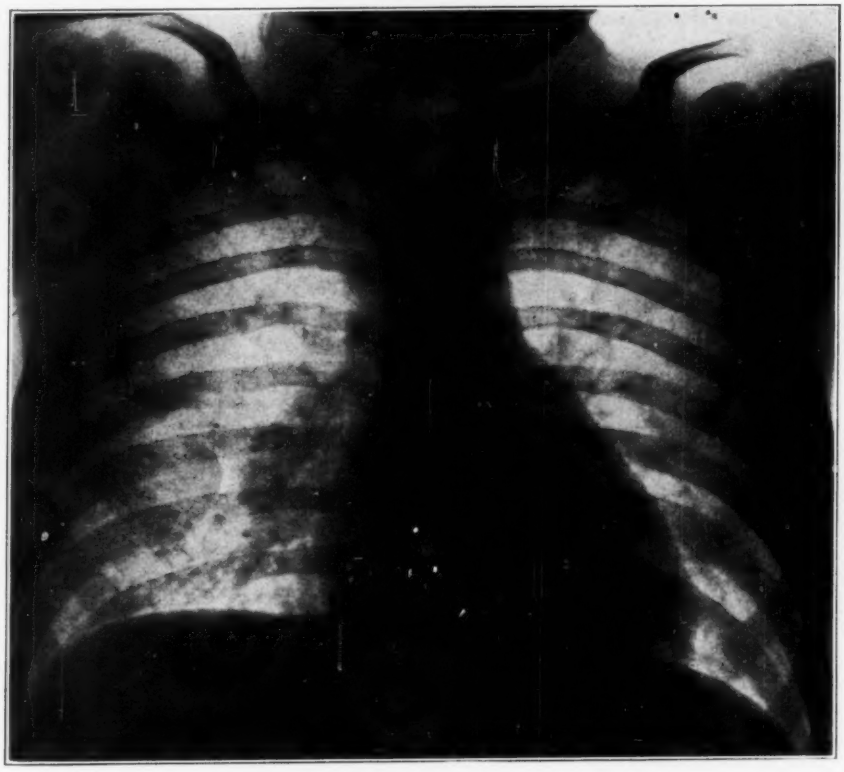

Fig. 35.—Miliary tuberculosis.

a dense shadow along the costal margin, and may push the lung in for a considerable distance. The diaphragmatic angle is obliterated, and the heart and mediastinum may be pushed to the opposite side. The shadow cast by fluid is more or less dense (Figs. 36-38), the structural markings gradually disappearing as the fluid becomes more and more of a thickened purulent character.

Encapsulated fluid may be seen in any part of the chest where there are opposing pleural surfaces. The outline of the fluid is quite definite, and the shadow is dense and free of lung markings. Thickened pleura may cast a shadow somewhat similar to a small amount of fluid.

Pneumothorax gives rather characteristic roentgenographic findings. The lung is compressed and pushed away from the thoracic wall. The air gives a transparent appearance to that portion of the chest, no structural markings are seen, and the edge of the collapsed lung is regular and sharply defined (Fig. 39).

Foreign bodies in the respiratory tract of children are of common occurrence. In relation to their examination by the roentgen ray, they may be divided into two classes: opaque and nonopaque. The nonopaque bodies in-

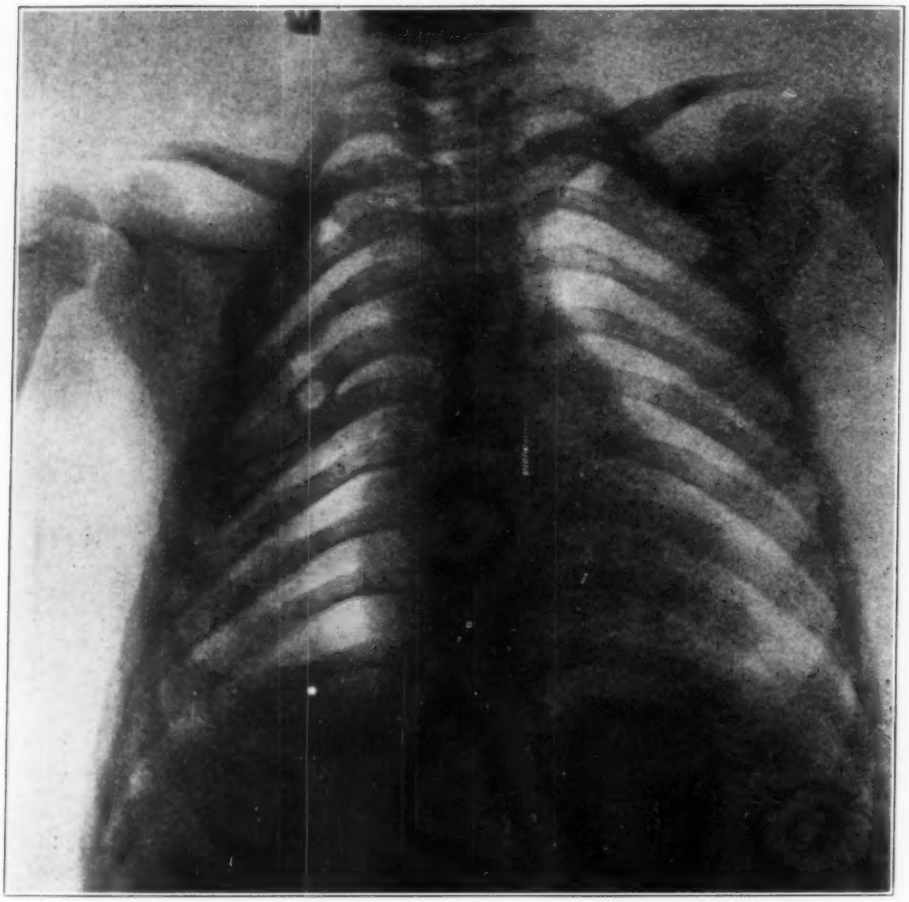

Fig. 36.—Postoperative pleural empyema on the right side, showing bridging of two ribs around drainage tube.

clude peanuts, beans, seeds, and nut shells. The opaque are chiefly metallic.

The radiographic findings vary, depending on the position and nature of the resulting obstruction. A monolateral emphysema results when the foreign body has passed the bifurcation, and is of such nature as to cause obstruction to the expiratory current. This is evidenced by the increased transparency of the affected area and depression of the diaphragm with partial fixation on that side. The heart and mediastinum are displaced away from the affected side, and there is increased excursion of the diaphragm

on the opposite side. When the foreign body completely obstructs the bronchus to ingress and egress of air, the residual air is quickly absorbed and atelectasis results. There is marked density of the shadow of the area involved. The heart and mediastinum are displaced toward the affected side. The diaphragm is retracted upward. Metallic objects cast a shadow and their detection is much less difficult.

Fig. 37.—Empyema.

It is of the greatest importance to take roentgenograms at the end of full inspiration and at the end of expiration in order to show the above changes. The fluoroscope should always be used in the examination of these cases, and is of the greatest assistance in their removal.

HEART CONDITIONS

The heart shadow in children does not differ greatly from that of adults (Fig. 32). In infants the size of the heart in relation to the chest is increased.

Congenital hearts do not always show demonstrable findings. Often enlargement of the pulmonary artery may be demonstrated. Alterations in the normal heart curve indicate a pathologic condition of the heart (Fig. 40).

Pericardial effusion casts an increased shadow, which tends to be pear-

Fig. 38.—Encapsulated empyema (encysted).

shaped (Fig. 41). Cardiac enlargement is often demonstrated by the roentgenogram. The fluoroscope is used to advantage in both of these conditions. For actual measurement of the cardiac outline, distance plates are taken in order that the shadow cast may be of actual size.

OTHER THORACIC CONDITIONS

Persistent thymus may be demonstrated by a homogeneous shadow extending downward from the clavicles on either side of the midsternum (Fig. 42). The width and extent of this shadow depend on the size and shape of the thymus.

The roentgen ray has also been found to be effective in the treatment of these cases. Overexposure, however, is to be avoided, because of the danger of skin burns, deleterious effect on the thyroid, and too rapid atrophy of the thymus.

Thoracic tumors are rare. Suffice it to mention the dense shadow which they cast, and the frequency of their origin from the mediastinum.

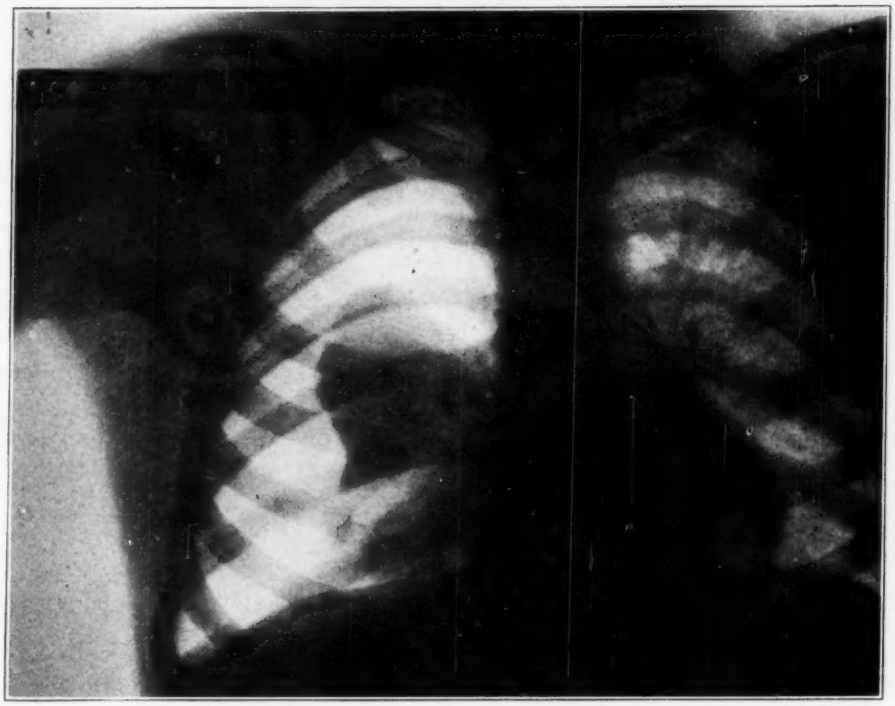

Fig. 39.—Right pneumonothorax with complete collapse of lung.

GASTROINTESTINAL CONDITIONS

In pyloric stenosis of infancy, and in other cases of persistent vomiting, the diagnosis may be expedited by following the course of an opaque meal, as shown by the fluoroscope and roentgenogram. The large dilated stomach, the thickened wall, the hyperperistaltic waves, and the reversed peristalsis may all be demonstrated. The percentage of the bismuth meal that passes the pylorus in a given time is indicative of the patency of the pylorus (Fig. 43). When one-half to two-thirds of the meal passes the pylorus in three hours, the immediate need of surgical interference is not indicated, and the condition, at most, is one of partial obstruction. If the bismuth is entirely re-

tained in the stomach after 4 hours there is complete obstruction of the pylorus and operation is indicated. Bismuth subcarbonate and barium are the salts most frequently used. They may be given in a small feeding in amounts of one-half to one ounce shortly before the examination is begun.

The information obtained by the observation of an opaque enema, by means of the roentgen ray, is of importance in cases of dilated colon and

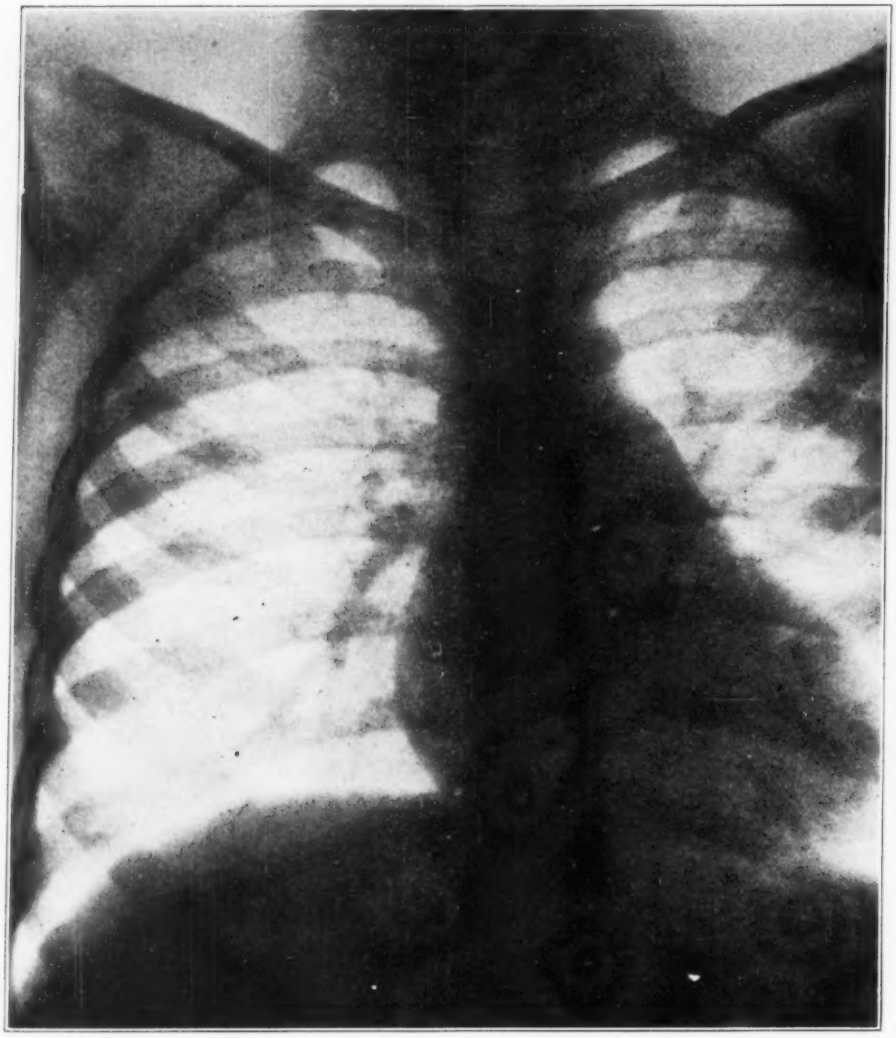

Fig. 40.—Pathological heart showing projection of left pulmonic curve.

Hirschsprung's disease. The increased diameter, looping, and any increase in length may be seen. Congenital malformation may be demonstrated, but not often. Tumors of the intestinal tract, as well as other tumors in the abdomen, may be seen at times if they are of sufficient size and density.

Calculi in the kidneys, ureters, and bladder may be shown in the roentgenogram. The examination of the urinary tract by means of opaque in-

jections may be done, but it is not frequently carried out because of the added dangers and difficulty of the operation. Dilatation of the pelvis of the kidney, dilatation of the ureters, and diverticula of the bladder may be demonstrated by this procedure.

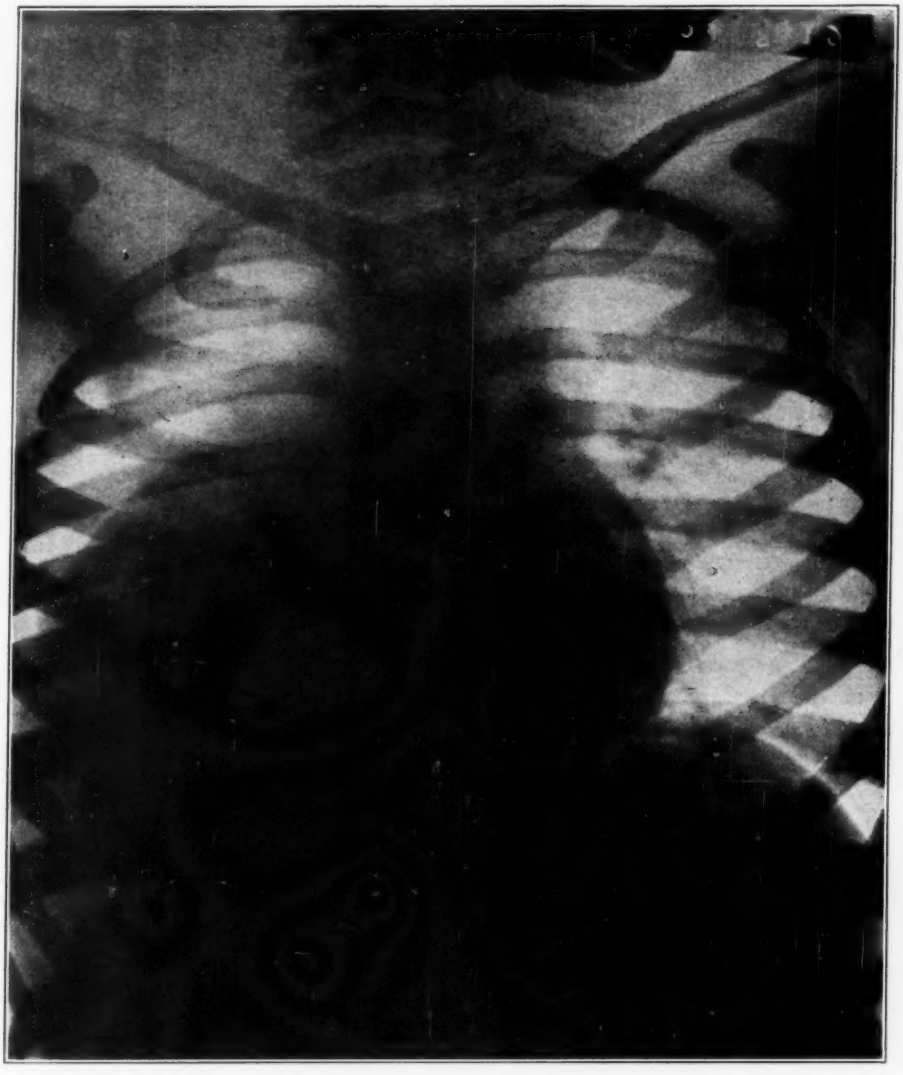

Fig. 41.—Precarditis with effusion.

The roentgen ray examination of the mastoid, nasal sinuses, and teeth is of service in older children. The late development of the sinuses in children, makes their examination less frequently necessary.

BONES AND JOINTS

Tuberculosis of the bone may be said to involve the epiphyses. Tuberculosis of the shaft is seen, but is rare. Tuberculous dactylitis is frequently seen

in tuberculous children and it may be impossible to differentiate the lesion from that of lues or osteomyelitis. Syphilis tends to involve more than one bone, and bone production is increased. Periostitis, and even tertiary lesions are often demonstrable in the roentgenogram. The serological tests and clinical course help to establish a definite diagnosis.

The most important differential points in the diagnosis of chronic bone and joint conditions in children may be summarized as follows:

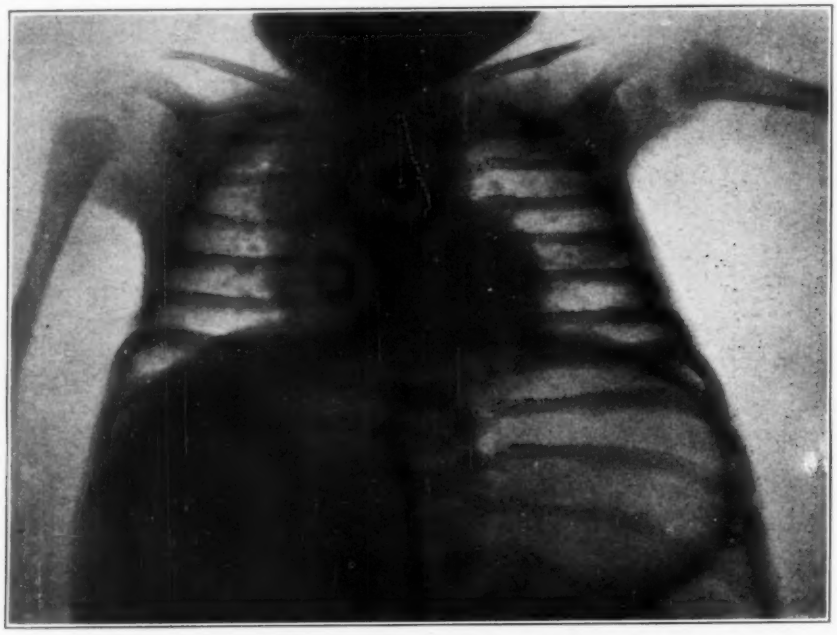

Fig. 42.—Persistent thymus. Broad superior mediastinum.

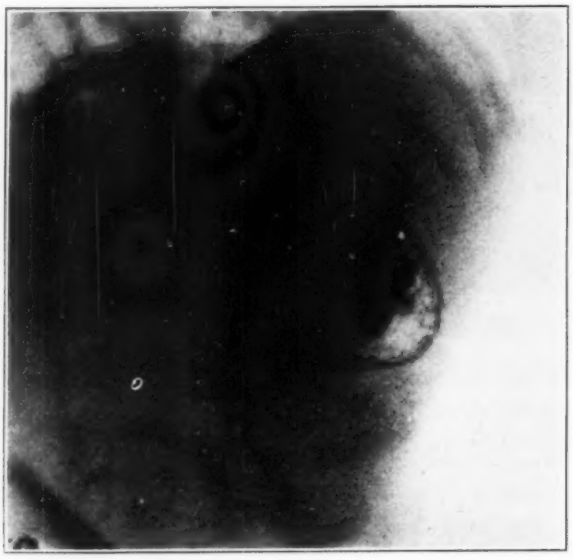

Fig. 43.—Pyloric stenosis showing gastric retention after four hours.

RICKETS.—

a. Multiple involvement.

b. Early the diaphysis is frayed out and no longer clear cut.

c. This becomes more marked, and there is a dense shadow cast by the margin, which becomes wider, and has an inverted saucer-shaped appearance (Fig. 44).

d. Atrophy is often present, and fractures not uncommon.

e. In old cases, dense, transverse, linear shadows may be seen in the diaphysis, indicating a nutritional disturbance when the epiphysis was at that point.

CONGENITAL SYPHILIS.—

a. No spreading out of the epiphyseal line.

b. No atrophy.

c. Periostitis usually present and extensive. It is laminated and is usually found on the lower third of the fibula and radii.

SCURVY.—

a. Epiphysis and epiphyseal line undisturbed.

b. "White line," 1-2 millimeters behind the epiphyseal line, extending over the entire bone outline (Fig. 45).

c. Subperiosteal hemorrhage nearly always present but may not be seen in the skiagraph.

d. Epiphyseal separation may be present.

TUBERCULOSIS.—

a. Most often confined to one joint.

b. Cartilaginous destruction is noted by the narrowing of the joint space.

c. Irregular, worm-eaten appearance, and general cloudiness.

PERTHES' DISEASE.—

a. Limited to the hip joint.

b. No cloudiness, bone detail clear cut.

c. The epiphysis, seems more flattened, denser than normal, and is not eroded or worm-eaten.

CHRONIC ARTHRITIS (Still's Disease).—The roentgenograph shows a thickening of the periarticular tissues, often distention of the joint. Osteoporosis may be noted.

OSTEOGENESIS IMPERFECTA.—There is decreased bone density; shortening of the long bones is present. Multiple fractures are nearly always present.

CHONDRODYSTROPHY.—There is marked shortening of all of the long bones. These give normal or increased shadows. The shortening is so marked as to cause little difficulty in the recognition of the condition.

Bone infections are frequent in children. Osteomyelitis is frequently acute. It is characterized by rapid bone destruction without bone regeneration (due to its rapidity).

The clinical findings may be such that a positive diagnosis can be made before any changes are seen in the roentgenogram. The earliest findings may

be seen as areas of decreased density in the medullary cavity; later, when the infection has traveled into the cortex, areas of decreased density may be demonstrated. In less acute and in chronic cases, bone destruction and regeneration may be seen (Fig. 46); still later, the sequestrum may be shown.

Bone Injuries.—Epiphyseal separation and injuries are frequent. The epiphyses at birth are for the most part cartilaginous, and are, therefore, not seen

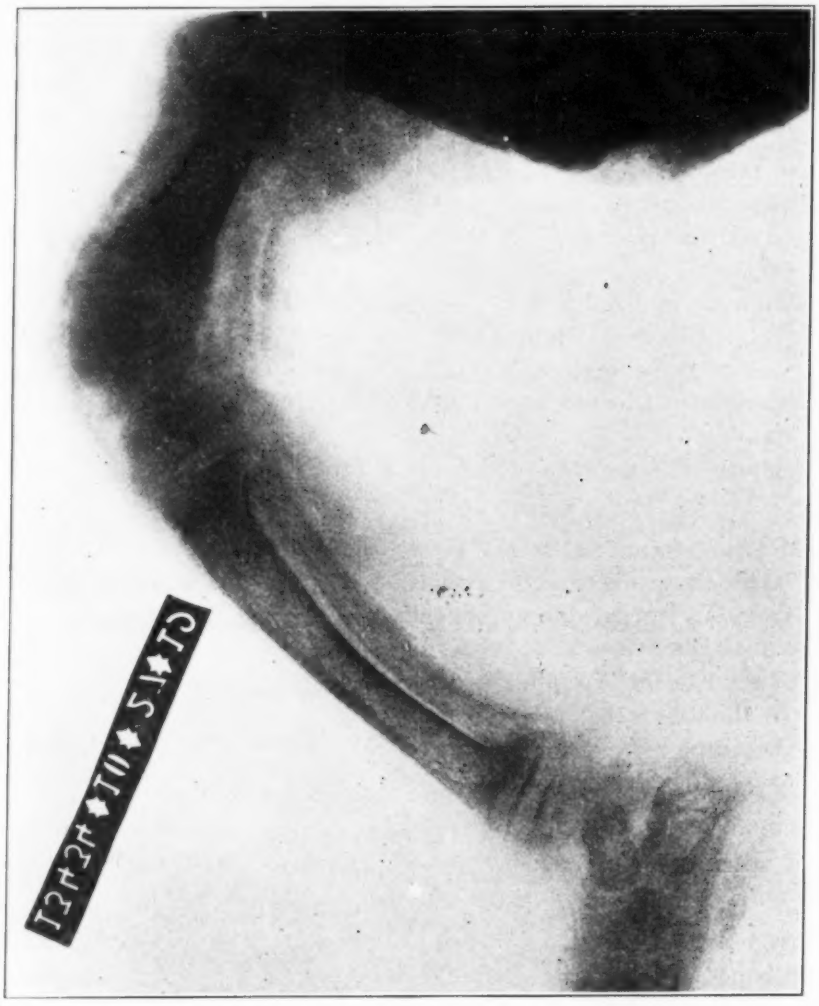

Fig. 44.—Rickets, showing flaring out of ends of the long bones.

in the roentgenograph. Nutritional disturbances delay the appearance and development of the epiphyses. In roentgen ray examination it is of the greatest importance to know the time of the appearance of these ossification centers.

In children, when the force of an injury centers at the epiphysis, epiphyseal separation occurs more often than fracture. Fractures in children are often of the green-stick variety, due to the tendency of the bones to bend. The

frequency of epiphyseal injury in children, and the difficulty in their recognition, both clinical and by the roentgen ray, must be kept in mind in the diagnosis and treatment of injuries about the joints. Corresponding parts should always be examined, and the two compared, in order to determine the extent of the injury. Antero-posterior, and lateral skiagraphs should be taken. The parts to be examined should be in close proximity to the film, or plate, in order to be as little distorted as possible.

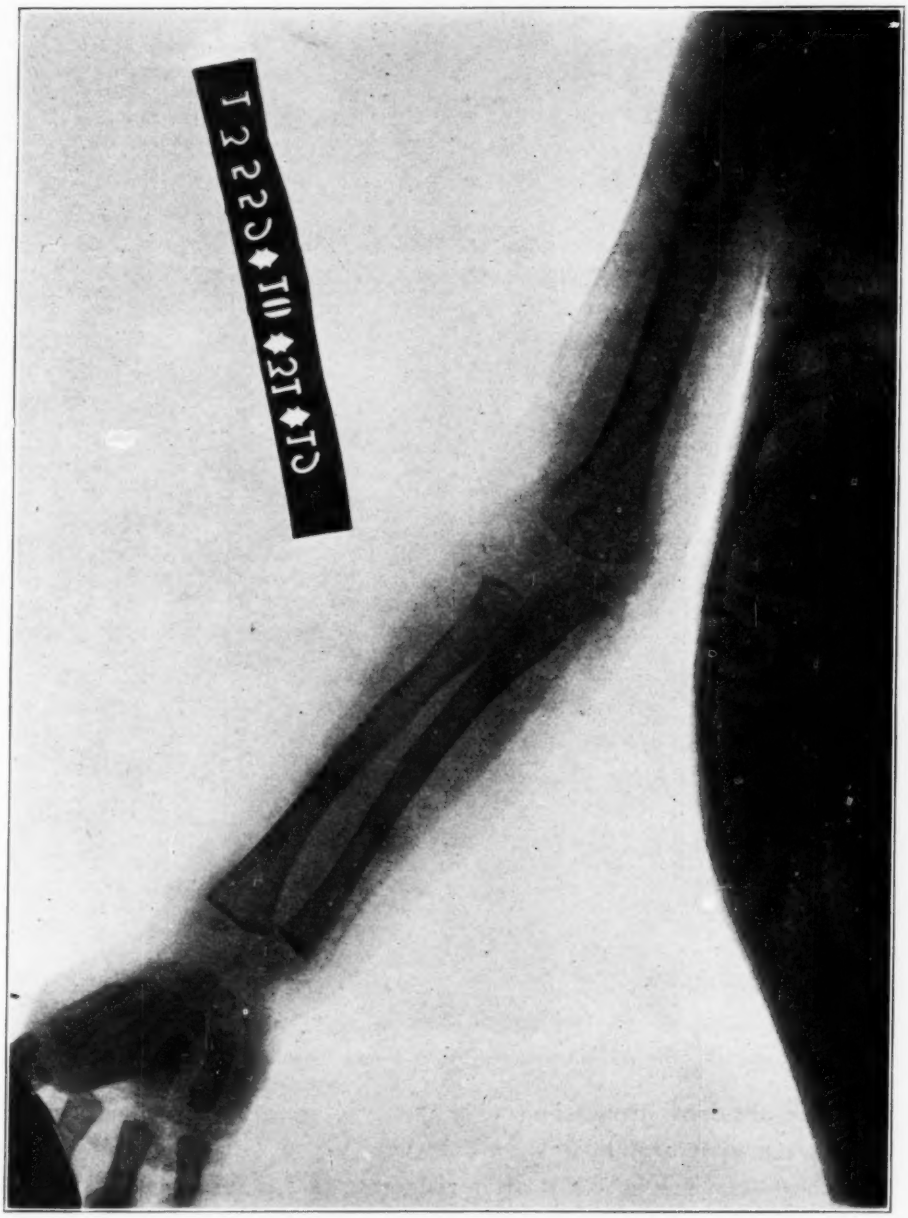

Fig. 45.—Scurvy showing the characteristic white line bordering the long bones (the line shows black in reproduction).

Of the congenital dislocations the hip and shoulders predominate. Congenital dislocation of the hip is often unnoticed until the child begins to walk, and it may be some time before any notice is taken of the waddling gait. In the roentgenogram, the shape of the pelvis, and the position of the head and neck of the femur in comparison with the normal side may make the diagnosis

Fig. 46.—Osteomyelitis of tibia with almost complete destruction.

clear. The acquired dislocations usually occur in later childhood, and the findings are similar to adult dislocations.

The roentgen ray is useful after reduction of fractures and dislocations has been made to determine the correctness of the parts as to apposition and alignment.

TABLE XIV

DEVELOPMENT AND UNION OF SOME OF THE MORE FREQUENT EPIPHYSES

LOCATION	APPEARANCE		UNION
Humerus, head	6-8 mo.	fuse at about 6 yr.	17-18 yr.
trochanters	3-4 yr.		
capitellum	1 yr.		
Internal condyle	5 yr.		
trochlea	10-11 yr.		
External condyle	12-14 yr.		
Radius			
Lower epiphysis	2-3 yr.		17 yr.
Olecranon	8-9 yr.		17-18 yr.
Femur, head	2-3 yr.		17-18 yr.
Lower epiphysis	at birth		18-20 yr.
Tibia, lower epiphysis	2-3 yr.		17-18 yr.

(To be continued.)

INVESTIGATIONS ON THE DOUBLE TYPE OF THE RECEPTORS IN THE TYPHOID-PARATYPHOID GROUP AND THEIR SIGNIFICANCE FOR THE WIDAL REACTION*

By Arthur M. Fishberg, M.D., New York

INVESTIGATIONS of recent years have shown that bacteria,[1] as well as other cells, for example sheep's erythrocytes,[2] may function as antigens through the simultaneous participation of a multiplicity of chemically distinct receptor groups. Apart from such investigations of *chemical* differences, Joos[3] found in many bacteria, particularly typhoid bacilli, two *serologically* differentiable agglutinogens. He separated them by heating to 60° C. to 62° C., at which temperature one of these agglutinogens was destroyed, while the other was unaffected by subjection to it for even several hours. Joos also noted that the flakes produced by the agglutination of the thermolabile antigen were coarse while those resulting from the thermostable fraction were fine. These investigations of Joos did not attract the attention they deserved, probably largely because heating to 62° C., as he recommended, is often insufficient to destroy the thermolabile agglutinogen.

It was first the studies of Weil and Felix[4] and their coworkers that showed the importance of closer analysis of the agglutination reaction than had previously been made. Working with proteus bacilli, they succeeded in serologically delimiting two proteus groups which they had isolated from typhus patients (the so-called X-strains) from one another and from the vulgar proteus strains. Weil and Felix found that the X2 and X19 strains have identical *thermolabile* but *different thermostable* receptors. Consequently, after destroying the thermolabile receptors by heating, it is immediately possible to serologically differentiate these two strains, though differentiation by an immune serum cannot be effected on bacilli with intact thermolabile receptors.

As a result of these investigations of Weil and Felix, and the subsequent ones of Schiff,[5] H. Sachs,[6] and others, it is now well established that in the typhoid, paratyphoid, Gärtner, and proteus groups, there are two groups of receptors, one of which is destroyed by heating to 100° C. for an hour, while the other is not affected by even a longer subjection to this temperature (in our experiments we have often heated to 100° C. for more than two hours without damage to the stable receptors). The agglutination of the thermostable antigen occurs in *fine* compact flakes which on sinking to the bottom of the tube form a compact sediment. On the other hand the action of the specific agglutinins on the thermolabile receptors results in *coarse*, rather loose flakes which form a bulky loose sediment, so that, in most

*From the Bacteriology Institute of the Krankenhaus in Friedrichshain, Berlin, Germany. Received for publication March 20, 1923.

cases, with a little practice one can tell from the appearance of the agglutination whether the thermolabile or the thermostable antigen is being carried down. For this purpose a hand lens is usually necessary, though a so-called agglutinoscope (Kuhn and Woithe) is preferable. When both types of flocculi are present in the solution, simple inspection often does not suffice, and recourse must be had to absorption experiments (see below). We have found the time factor a great aid in differentiation. The coarse agglutination occurs much more rapidly than the fine, being usually complete (with typhoid bacilli) in less than half an hour. On the other hand the fine agglutination may require several hours to attain completion. It is not uncommon in following the progress of an agglutination reaction to initially observe what is apparently a purely coarse agglutination which is later complicated by the appearance of fine flakes also.

Analysis of the receptor apparatus in the typhoid-paratyphoid-Gärtner group by means of absorption experiments on artificial immune sera has been carried out by Weil and Felix, Schiff, and others. We have also made such experiments, using the stock strains in the laboratory, and have arrived at essentially the same results, which are as follows: The three varieties of bacteria have thermostable receptors in common, but the thermolabile receptors are specific. The thermostable receptors of typhoid and Gärtner bacilli are qualitatively identical. Paratyphoid B has thermostable receptors which are identical with those of the other two but has also specific receptors of this type. The following schema indicates these relationships:

	THERMOSTABLE RECEPTORS	THERMOLABILE RECEPTORS
Typhoid	AB	a
Paratyphoid B	AC	b
Gärtner	AB	c

To the thermolabile and thermostable agglutinogens correspond two different agglutinins, designated by Schiff as labilotropic (the coarse-flaking) and stabilotropic (the fine-flaking) agglutinins. In an ordinary typhoid immune serum both agglutinins are present, but their quantitative relationships may vary greatly. As a rule, in the highest dilutions still causing agglutination the effect is due to the labilotropic antibodies; i.e., the labilotropic end titer is higher than the stabilotropic. Rather uncommonly the reverse is true. Purely fine-flaking typhoid immune sera can be obtained by immunizing with typhoid bacilli that have been heated to 100° C. sufficiently long to destroy the thermolabile agglutinogens. Or such a serum can be prepared from an ordinary immune serum containing both types by absorbing the stabilotropic agglutinins with bacilli heated to 100° C. for an hour or more.

As yet the thermolabile agglutinogens have been found only in bacteria with well developed flagella. It has, therefore, been suggested that the thermolabile receptors are contained in the flagella, or at least intimately associated with their presence.[7] Hence the agglutination type is of no significance for the diagnosis of infections with dysentery bacilli, the cocci, etc., but it might very well be supposed, *a priori*, that it would be worthy of

consideration in the agglutination test for typhoid fever. I have, therefore, with the kind cooperation of Dr. Fritz Schiff, Director of the Bacteriological Institute of the Krankenhaus im Friedrichshain, Berlin, investigated the types of agglutinins in the sera of typhoid and paratyphoid patients and their importance for the diagnosis of the disease.

The following were the points investigated:

(1) To which type the agglutinins of normal serum belong.

(2) The type of the agglutinins in the sera of typhoid patients.

(3) The significance of the receptor types for the technical details of the Widal reaction.

(4) The significance of the agglutination type for differential diagnosis.

(5) The type of the agglutinins in the paratyphoid infections.

(1) THE AGGLUTININS OF NORMAL SERA

It is a well known phenomenon that typhoid bacilli are sometimes agglutinated by the serum of individuals who have neither typhoid fever at the time of the examination nor a history of a previous typhoid infection or vaccination. In the course of our investigation we studied 60 normal sera. About 20 per cent of these sera in concentrations of 1:20 agglutinated typhoid bacilli. In three cases the agglutination was still present at a dilution of 1:50. These results were obtained when the reaction was read after two hours; if the reading was carried out after twenty-four hours most of the normal sera caused at least slight agglutination in the very high concentrations. But in every case the agglutination was in *fine flakes*, that is, *the normal agglutinins are stabilotropic* (fine-flaking), and can be completely absorbed from the serum by typhoid bacilli which have been heated to 100° C. for one hour, as is shown, for example, in the following protocol:

Serum 1083, diagnosis syphilis of the liver. A 24-hour agar plate culture of typhoid bacilli was suspended in physiological salt solution and heated on the water-bath to 100°C for one hour, centrifuged, the supernatant fluid poured off, and 5 c.c. of 1:10 dilution of the serum added to the sediment. After mixing, it was put in the incubator at 37°C for 15 minutes, again centrifuged, the supernatant serum poured off and used for the agglutination. All subsequent absorption experiments were carried out similarly. But in doing such experiments it should be borne in mind that complete absorption from strong, concentrated sera is difficult, so that it is better to carry out the absorption on higher dilutions of concentrated sera, and repeat it once or even twice.

SERUM DILUTION	UNTREATED SERUM WITH		ABSORBED SERUM WITH	
	Living typhoid bacilli	Typhoid bac. heated to 100° 1 hour	Living typhoid bacilli	Typhoid bac. heated to 100° 1 hour
1:10	++ fine	+ fine	—	—
1:20	+ fine	(+) fine	—	—
1:50	(+) fine	(+) fine	—	—
1:100	—	—	—	—
1:250	—	—	—	—

Reading after two hours. Plus signs in parentheses mean that the agglutination could only be determined with certainty with the aid of the agglutinoscope.

All our other analyses of agglutinating sera from nontyphoid patients gave similar results, so the following conclusions seem justifiable:

(1) A coarse agglutination is not due to the normal agglutinins.

(2) If the agglutinins for typhoid bacilli cannot be removed from a serum by absorption with these bacilli heated to 100° C. for one hour (observing the precautions, with concentrated sera, mentioned above), the agglutination is not due to normal agglutinins. But the converse is not necessarily true, i.e., a purely fine agglutination may be brought about by the serum of a typhoid patient (see below).

(3) Since stabilotropic (fine) agglutination occurs much more slowly than labilotropic, normal sera are far more likely to give an apparently positive agglutination test if the reading is done after twenty-four hours than if carried out after one or two hours.

Of four icteric sera (which are often stated to give quite frequent positive Widals,) one gave a positive reaction in a dilution of 1:50. It was typically stabilotropic (fine), and as a matter of fact there was no indication of typhoid in the history.

(2) THE AGGLUTININS IN TYPHOID FEVER

We investigated the sera of 31 patients suffering from typhoid fever of all stages. Their content in stabilotropic agglutinins was determined by

TABLE I

SERUM	LABILOTROPIC TITER	STABILOTROPIC TITER
2144	1:1000	1:2000
71 V	1:250	1:250
B 41	1:1000	1:100
2284	1:2500	1:500
2184	1:200	1:20
2206	1:1000	1:250
2255	1:2500	neg. in 1:50
2252	1:2500	1:100
2258	1:2500	1:400
3083	1:500	1:250
3121	1:500	1:100
3209	1:50	neg. in 1:10
3212	1:1000	1:100
3215	1:2500	1:1000
3220	1:250	1:50
3221	1:250	neg. in 1:10
3228	1:100	1:10
3254	1:250	1:50
3258	1:500	1:100
3226	1:750	1:50
3180	1:100	1:1000
3197	1:100	1:50
3203	1:250	neg.
3232	1:100	1:10
3240	1:500	1:1000
2266	1:1000	neg.
2179	1:200	neg. in 1:10
2283	1:2500	1:250
R	1:250	1:50
2068	1:5000	1:5000
3126	1:1000	1:25

Reading in all cases after 24 hours.

agglutination experiments with typhoid bacilli heated to 100° C. or with Gärtner bacilli, whose thermostable receptors we have seen to be identical with those of the typhoid bacillus. The labilotropic titer could be taken as identical with the titer of the entire serum when the latter was higher than the stabilotropic titer. In cases of doubt it was determined by first absorbing the stabilotropic agglutinins with heated bacilli. Table I shows the titer of the sera of typhoid patients in both types of agglutinins:

From this table we can see that while all the typhoid sera contained labilotropic agglutinins, six (almost 20 per cent) were lacking in the stabilotropic type. In but three cases was the stabilotropic titer the higher, in two the titers were equal, while in the remaining 26 the labilotropic titer was the higher.

In a case which was studied from an early stage (before the Widal reaction became positive) to death, no relation of the agglutinin type to the stage of the disease could be discerned.

(3) SIGNIFICANCE OF THE RECEPTOR TYPES FOR THE TECHNICAL DETAILS OF THE WIDAL REACTION

(a) *Time of Reading.* Labilotropic agglutination occurs very rapidly, so that sera in which these agglutinins predominate (as they do in the large majority of cases) can be read very soon. Agglutination of this type is usually almost completed within half an hour, and practically always within two hours. On the other hand, if the serum contains largely stabilotropic (fine) agglutinins, agglutination may not be complete for many hours, so that reactions negative at the end of two hours should always be seen after 24 hours. But in interpreting these late (almost always predominantly fine) agglutinations, it should always be recalled that the normal and the partial agglutinins are fine. Agglutination present at half an hour is, on the contrary, in the large majority of cases coarse and therefore almost surely specific.

(b) *Selection of the Strain.* Weil and Felix[8] analyzed the receptors of many strains of typhoid bacilli and found little variation in the thermolabile receptors of the different strains, but very considerable fluctuations in the agglutinability of the thermostable receptors; some strains showed practically no stabilotropic (fine) agglutination. Hence, in the selection of a strain for routine Widal reactions, care should be taken to obtain one with functioning thermostable receptors, or positive agglutinations with sera whose agglutinins are largely stabilotropic may fail of detection. The thermostable receptors of a strain are tested by heating the bacilli to 100° C. for one hour and then seeing how well they are agglutinated by an artificial immune serum known to contain both types of antibodies.

(c) *Use of a "Typhoid Diagnosticum."* The diagnosticum must be prepared so that it contains both types of receptors. We have tested the Ficker Diagnosticum, which is widely used, and found that it does contain both varieties of receptor. In our experiments we have found, as did Weil and Felix, that alcohol destroys the labilotropic agglutinins, and therefore typhoid

bacilli which have been treated with alcohol for 24 hours and then suspended in salt solution act as do heated bacilli, and may be used for the detection of the stabilotropic agglutinins alone.

(4) SIGNIFICANCE OF THE AGGLUTINATION TYPE FOR DIFFERENTIAL DIAGNOSIS

In carrying out the Widal reaction it not rarely occurs that the end-titer of the serum for typhoid and paratyphoid B. is so nearly the same that it is impossible to say, in the absence of a positive culture, which is the infecting organism. Consideration of the agglutination type may be of great aid in such a dilemma. If early inspection (after 10 to 15 minutes at 37° C.) of the tubes containing typhoid bacilli shows a labilotropic (coarse) agglutination, the infecting organism is the typhoid bacillus for, as we have seen, the normal agglutinins are stabilotropic and the typhoid-paratyphoid group have in common only some stable receptors. But it is to be emphasized that absence of coarse agglutination with typhoid bacilli does not absolutely exclude a typhoid infection for there are rare typhoid sera containing almost exclusively stabilotropic (fine) agglutinins, though we did not encounter in our series of 31 cases, any totally lacking in stabilotropic antibodies. Naturally, in paratyphoid infections the coarse agglutination is found in the tubes containing paratyphoid bacilli, the agglutinins for typhoid bacilli, if any, being fine-flaking.

For purposes of differential diagnosis in the typhoid-paratyphoid infections Castellani's absorption experiment is used considerably, but often fails to attain its goal. The conditions for its success or failure can be explained by consideration of the receptor types. In the typhoid-paratyphoid Gärtner group the thermolabile (coarse) receptors are, with rare exceptions, specific, while many of the thermostable (fine) receptors are possessed in common by the three varieties of bacteria, in fact the thermostable receptors of typhoid and Gärtner bacilli are entirely identical. Hence, differentiation of sera from typhoid and Gärtner bacillus infections by means of absorption experiments is only possible when the labilotropic agglutinins are present in sufficient concentration. The Castellani absorption method will differentiate paratyphoid infections when the labilotropic agglutinins are abundant, but not always when the stabilotropic predominate.

(5) THE AGGLUTININS IN THE SERA OF PARATYPHOID B. INFECTIONS

The sera of four patients suffering from paratyphoid B. infections were investigated. All of these infections were of the typhoid form, there being no sera of cases of gastro-enteritis due to paratyphoid bacilli. These sera were tested as to their ability to agglutinate paratyphoid B. bacilli, paratyphoid B. bacilli that had been heated to 100° C. for one hour, typhoid bacilli, and the Aertryck strain of paratyphoid B., which is a cause of infectious meat poisoning. Similar tests were carried out on the sera after their stabilotropic agglutinins had been removed by absorption with paratyphoid B. bacilli that had been heated to 100° C. for one hour. Table II shows the results:

TABLE II

SERUM OF PATIENT	TITER OF UNTREATED SERUM FOR			
	Paratyph. B	Heated Paratyph. B.	Aertryck	Typhoid
Gr.	1:1000 c. & f.	1:250 f.	1:250 f.	1:1000 f.
Ch.	1:500 c. & f.	1:50 f.	1:250 f.	1:100 f.
B.	1:2500 c. & f.	1:1000 f.	1:500 f.	1:500 f.
K.	1:250 c. & f.	1:10 f.	neg.	neg.
		Titer of serum after absorption:		
Gr.	1:500 c.	neg.	neg.	neg.
Ch.	1:500 c.	neg.	neg.	neg.
B.	1:2500 c.	neg.	neg.	neg.
K.	1:100 c.	neg.	neg.	neg.

c = coarse, f = fine. Reading after 24 hours.

The above results demonstrate that the sera of these four patients infected by paratyphoid B. contain both labilotropic and stabilotropic agglutinins for the infecting organism, but that the partial agglutinins are fine and can be removed from the serum by absorption with heated paratyphoid B. bacilli. These experiments also confirm the previous results of Schiff, who found that the ordinary strains of paratyphoid B. bacilli differ from the strains causing acute gastroenteritis (Breslau, Aertryck, etc.) in their thermolabile receptors, though the thermostable fractions are identical. So that to the striking differences in the clinical courses of the two main groups of paratyphoid B. infections there correspond definite serological differences between the respective infecting organisms.

I should like to express my thanks to Privat Dozent Dr. Fritz Schiff for many courtesies extended in the course of this investigation, as well as to the Robert Koch Institute and the Bacteriological Laboratories at Kiel and Greifswald for sera kindly placed at my disposal.

RECAPITULATION

1. The receptors of the typhoid-paratyphoid-Gärtner group are of two types—thermolabile and thermostable. To each agglutinogen corresponds a specific agglutinin, termed respectively labilotropic and stabilotropic.

2. Agglutination of the thermolabile antigen occurs in coarse flakes, of the thermostable in fine flakes.

3. When typhoid bacilli are agglutinated by the serum of a patient who has never had typhoid fever, the agglutination is of the fine type.

4. Partial agglutination in the typhoid-paratyphoid-Gärtner group is of the fine type.

5. All our sera giving positive Widal reactions—31 in number—contained labilotropic agglutinins, 26 of the sera also contained stabilotropic agglutinins.

6. We did not encounter any coarse agglutination reactions brought about by sera of other than typhoid patients. The "nonspecific Widals" showed the fine type of agglutination.

7. Consideration of the receptor type is of significance for the technical details of the Widal reaction, particularly the time of reading and the choice of the strain employed, as well as for the Castellani experiment.

8. Sera from patients suffering from the typhoidal form of paratyphoid-B. infection contain both stabilotropic and labilotropic agglutinins for the usual strains of paratyphoid-B. bacilli, but only stabilotropic agglutinins for typhoid bacilli and for these strains of paratyphoid-B. (Aertryck, etc.) which cause acute gastroenteritis.

REFERENCES

[1]See E. P. Pick, Kolle-Wassermann's Handbuch, ed. 2, 1912, i, 779.
[2]Forssman, Biochem. Zeitschr., xxxvii, No. 11; Friedemann, Biochem. Zeitschr., lxxx.
[3]Central. f. Bakt., Abt. I, Orig. lxxxiii, 1903, 762.
[4]Wien. klin. Wchnschr., 1917, No. 48, 1918, No. 23 and 36, Zeitschr. f. Immunitätsf., Orig. 1920, xxix, parts 1 and 2.
[5]Ztschr. f. Immuni., Orig. 1922, xxxiii, part 6.
[6]Deutsch med. Wchnschr., 1918, p. 459.
[7]See Braun and Schäffer, Berl. klin. Wchnschr., 1919, No. 12.
[8]Zeitschr. f. Immunitätsf., Orig. 1920, xxix, parts 1 and 2.

BACTERIOPHAGE PHENOMENA. II*

By Lloyd Arnold, M.D., Chicago, Ill.

WE have called attention in a previous paper in this journal[5] to the increased activity of a bacteriophage substance when added to a 3 hour old culture of a susceptible microorganism. This increase in virulency is very striking, leading in the majority of instances to complete sterilization of the culture. The same bacteriophage added in the same concentration to cultures of varying ages, ranging from 1 to 12 hours old, does not produce so marked a change as it does in the 3 hour old culture. In some few instances this takes place in either the 2 or the 4 hour old cultures, but usually it is found in the 3 hour old culture.

The life cycle of a bacterial culture may be conveniently divided into: (a) latent period; (b) period of maximum rate of growth or the logarithmic period; (c) stationary period; (d) period of decline. These phases are determined by estimations of the number of viable microorganisms present at various intervals. It is well known that these periods merge into one another without a sharp dividing line. The duration of these phases vary with the different species of bacteria, and even with the same microorganism under different environmental conditions.

By the latent period or lag is meant the interval which elapses between the time of inoculation and the time at which maximum rate of growth begins. The period was first recognized by Muller.[1] This varies from about 1 to 3 hours in duration, depending upon whether the bacteria have been accustomed to grow upon the medium used; the temperature, and upon other factors as yet unknown.

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The logarithmic period, is the phase of rapid growth during which the bacteria are dividing regularly; they increase in number in a standard unit of time, following the law of geometric proportion. This period varies from 2 to 8 hours in duration (Rahm,[2] Penfold,[3] and Chesney[4]).

The stationary period, is the phase in which the bacteria cease to multiply at a maximum rate; their increase in number becomes less and finally ceases. The duration of this period is much longer in time than either of the two previously mentioned phases. After expiration of several days, the period of decline begins, in which the number of living bacteria decreases.

After a short period of rest, the lag phase, there begins a logarithmic or maximum growth period; this can be thought of as a stimulation period. It is during this period that the bacteria multiply by geometric progression. It is during the beginning of this stimulation period that we find the bacteria most susceptible to the bacteriophage activity. The susceptibility is increased if the bacteriophage is added to the bacterial culture after incubating for three hours. If the bacteriophage is added at the time of inoculation of the culture, the same increase in virulency is found during the beginning of the logarithmic growth, but the activity decreases on further growth of the bacteria. On the other hand, if the bacteriophage is added after 3 hours' incubation, the culture usually becomes sterile almost immediately and remains so for several days or weeks. At the end of this logarithmic or stimulation period there is another biological change in the bacteria in their relation to the bacteriophage. The change does not take place so rapidly as during the beginning of this period, nor does it last for so long a period of time. The greatest bacteriolytic activity is not manifested until 24 or 48 hours after the bacteriophage has been added to a 7 to 10 hour old bouillon culture of the susceptible microorganism. After a few days this passes off and no bacteriolytic activity can be demonstrated in such cultures.

We think that the constant results we have obtained in reference to the 3 hour old culture is due to the fact that we have been working with this particular strain B. typhosus (Olsen) for two years and the numerous transplants, etc., that have been made in our laboratory; using the same medium, temperature, etc., has accustomed this microorganism to the extent that its lag and logarithmic periods are almost constant. In a later paper dealing with bacterial counts this supposition will be substantiated by experimental evidence.

In this paper we wish to deal with this question of the logarithmic period of growth and its influence on bacteriophage activity, by means of using the Berkefeld filtrate of cultures during this and other phases of the life cycle of B. typhosus.

EXPERIMENTAL

The same technic was used in these experiments as was described in the preceding paper.[5] The fourth extraction of a bottom water-agar layer was used, the original bacteriophage was obtained from the feces of a typhoid

patient. Five flasks of bouillon, each containing 150 c.c. were incubated overnight and then inoculated with 1 c.c. of an 18 hour old bouillon culture of B. typhosus (Olsen). After 3 hours incubation the contents of one flask was passed through a Berkefeld filter; after 6, 9, 24, and 48 hours' incubation the contents of the other four flasks, respectively, were pulled through Berkefeld candles. The filtrates were adjusted, under sterile conditions, to a hydrogen-ion concentration of PH 7.0°, then pipetted into bouillon in the concentration of 1:1 and 1:4; two series were used.

The results of these experiments were negative. There is very little variation occurring in the various filtrate series as compared with the control bouillon.

In the first series of experiments made, we did not adjust the hydrogen-ion concentration, and as a consequence we obtained different results. We are now confident that these results were due to a variation in the reaction of the medium and not to the influence of any bi-products of metabolism present in the filtrates due to bacterial growth. Rahm[2] found that the 4, 6, 8, and 12 day old Berkefeld filtrates of B. fluorescens liquefaciens bouillon cultures did not exert much influence upon the life cycle of this microorganism. It is probable that if the change in reaction had been corrected, the small change he observed would not have occurred. Penfold[3] found the filtrate of a 17 hour old B. coli in bouillon did not effect the lag period of this bacteria. The changes that one observes in the reaction between a susceptible microorganism and a bacteriophage seems to depend upon the bacteria itself. It is not due to the medium in which the bacteria is growing at the time this change takes place.

The majority of the workers who have studied the lag and logarithmic periods of growth, have come to the conclusion that the cause for this must be within the bacteria itself. (Penfold, Chesney, etc.) We think the bacteriophage reacts best with the bacteria at certain periods of its life cycle, namely, the beginning and the end of the logarithmic growth period, this is independent of biproducts of growth of the bacteria present in the medium at this time.

REFERENCES

[1]Mueller, M.: Z. Hyg. w. Infectionskrankh., 1895, xx, 245.
[2]Rahm, O.: Centralbl f. Bakteriol, etc. II Abt, 1906, xvi, 417, 609.
[3]Penfold, W. J.: Jour Hyg., 1914, xvi, 215.
[4]Chesney, A. M.: Jour. Exp. Med., 1916, xxiv, 387.
[5]Arnold, L.: Jour. Lab. and Clin. Med., August, 1923, viii, 720.

SUGAR IN URINE*

By Robert L. Thrasher and Charles W. O. Bunker

BENEDICT'S qualitative test[1] for sugar in urine has proved very useful and reliable, and we have been curious as to whether results from its use have any quantitative significance. The method of Folin and Berglund[2] for the estimation of sugars in normal urine offered a simple means of deciding the question, and we have applied it to 190 urines, 109 of which were negative by Benedict's tests, while 81 showed greenish turbidities. Depending upon the density of this greenish turbidity, we have subdivided the group into traces, slight traces and very slight traces. Table I shows the results.

It will be noted that 88 per cent of the negative results were with urines containing 0.1 per cent or less of sugars. No sharp line, however, could be drawn as to the amount of sugars that would or would not give a positive result, although there was a tendency for the density of the greenish turbidity to vary, in general, proportionately to the amount present. Neither did we find that the occurrence of a reddish precipitate that settled to the bottom of the tube had any quantitative significance.

Folin and Berglund[3] contend that the copper-reducing substances remaining in normal urine after the removal of coloring matters, uric acid, creatine, and creatinine by means of the alkaloidal reagent consist of a "motley variety of carbohydrate products and carbohydrate derivatives including di- and polysaccharides." If we consider that Benedict's test is sensitive to some of these but not to others, we can understand why values as low as 0.04 per cent could produce either a positive or a negative result, depending upon the composition of the mixture present in the urine. It may also be that the relative proportions of fermentable to nonfermentable copper-reducing substances enter into the question, but we did not attack it from that standpoint.

Since a positive result was obtained with as little as 0.04 per cent of sugar, Benedict's qualitative test must be considered as having at least that sensitiveness.

CONCLUSIONS

1. Benedict's qualitative test for sugar in urine has quantitative significance in only the most general terms.

2. Greenish tubidities secured in this test demand care in their interpretation, and are to be considered pathologic only when other features of the case warrant such an assumption.

*From the Laboratories of the U. S. Naval Medical School.
Received for publication, May 10, 1923.

TABLE I

MILLIGRAMS SUGAR PER 100 C.C. FOUND WITH THE FOLLOWING QUALITATIVE RESULTS

NEGATIVE	VERY SLIGHT TRACE	SLIGHT TRACE	TRACE
8			
10-11-11-13			
13			
20-22-23-23			
26-29			
31-32-33-35			
35-37-38			
40-40-40-40		40-42	
40-43-43			
43-43-46			
46-46-46			
47			
50-50-50-50			
52-53-53			
54-54-54			
54-57-57			
57			
60-60-60-60		66	
60-60-60			
63-63-63			
66-66-66			
66-66-66			
67			
70-71-71-72		75-75	71
72-73-75		70-70-75-75	
80-80-80-80	80	80-80-80-85	80-80-85
80-80-80		85-86-86	
85-85-85			
86-86-86			
86			
92-92-92	91-95	90-92-92-95	
		95-95	
100-100-100		100-100-109	104-109-109
100-100		109-109	
100-100		109	
109-109			
110-110-114			110-111-114
114			114
120-120-120		120	120-120-120
120			128-128
133-133-133		133-133-136	133-133
			142
150	150	150-150-150	150-150-150
			150 155
			163
			171-171-171
			171-177
			180-180-180
			188
		190	
			200-200
		218	
		240	224
			257-257
			500

BIBLIOGRAPHY

[1]Benedict, S. R.: Jour. Am. Med. Assn., 1911, lvii, 1193.
[2]Folin, O., and Berglund, H.: Jour. Biol. Chem., 1922, li, 209.
[3]*Ibid*, p. 213.

LABORATORY METHODS

ULTRAFILTRATION OF BLOOD SERUM AND CEREBROSPINAL FLUID WITH SPECIAL REFERENCE TO A NEW APPARATUS*

By Grete Egerer-Seham, Ph.D., Minneapolis, Minn.

SINCE Quincke, in 1891, brought the spinal puncture into clinical use the studies on the cerebrospinal fluid have greatly increased, especially since the introduction of accurate and sensitive microchemical and biological reactions. Notwithstanding, our knowledge of the physiology and pathology of the cerebrospinal fluid is still relatively incomplete.

It is commonly accepted that the fluid is derived from the blood and that its source is the chorioid plexus. How the fluid is formed and what rôle the chorioid plexus plays in its formation is, as yet, a matter of speculation. The exact nature of cerebrospinal fluid, i.e., whether it is an active secretion or a filtrate has never been determined.

McClendon has suggested that the cerebrospinal fluid is an ultrafiltrate of blood serum. He showed that a fluid could be produced by ultrafiltration of serum that resembled, in at least several physical and chemical characteristics, the cerebrospinal fluid. His work seemed to open a field of investigation that might prove fruitful.

This paper is concerned with the ultrafiltration of blood serum, special attention being given to the presence or absence in the ultrafiltrate of globulin, the colloidal gold curve and the Wassermann reaction.

The first problem was to devise an apparatus and method of ultrafiltration that would be as simple as possible and yet give accurate and quantitative results. The apparatus finally made and used is the one shown in Fig. 1. It is similar in principle to the one devised by Bechold, but much simpler in construction, rendering ultrafiltration comparatively easy.

The ultrafiltration apparatus described in this paper has the following advantages: (1) It allows as complete a quantitative ultrafiltration as can be expected. (2) The apparatus is easily constructed at a small expense. (3) The experiments can be carried out with great ease in relatively short time.

Fig. 1 shows the apparatus ready for use and Fig. 2 represents a cross section of the apparatus. It consists of an ordinary air pump (*A*) which is connected by means of a metal tube (*B*) to a gauge (*C*) from which a brass tube (*D*) leads to the apparatus proper (*E*). This apparatus (*E*) consists

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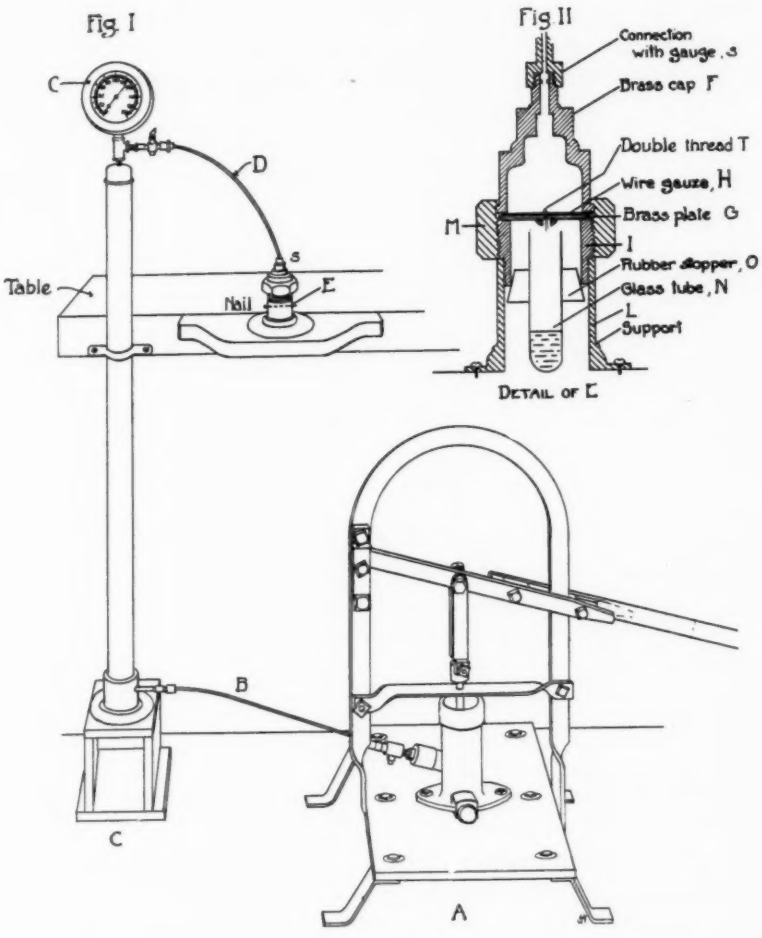
of an upper cap (*F*) made from brass tubing. This rests on a brass plate (*G*) 1½ inches in diameter, perforated in the center, a wire gauze of very fine mesh rests upon the brass plate occupying about 4/7 of the entire circumference. The edge of the gauze is on the same level with the rim of the brass plate. A double thread (*I*) taken from the same wire gauze is passed through the center of the gauze and through the perforation in the plate (*G*). The plate lies on the receptacle (*I*) made of brass tubing with two holes in juxta-



Figs. 1 and 2.

position. In order to screw together the cap (*F*) and the receptacle, a heavy metal nail is pushed through both lower receptacles (*I* and *L*). In order to avoid contamination of the fluid examined, certain parts of the apparatus (*F-H-I-G*) are coated with gold. Experiments are carried out in the following way:

Receptacle *L* is fastened to the table. It is sufficiently large to hold the receptacle *I* and it is perforated on either side like receptacle *I*. Part *I* is placed into the receptacle *L* and the nail is passed through the holes. The

filter plate *G* is placed upon the receptacle *I* and the wire gauze *H* is put over the plate with the wire thread passing through the pin hole. The filter paper 1½ inches wide, coated with collodion, is put on the wire gauze. A rubber washer of the same diameter as the brass plate is used. Lastly part *F* is placed on the rubber ring and the screw cap *M* that holds the parts together adjusted airtight with a wrench. A small glass tube (*N*) fitted with a bored rubber stopper (*O*) is employed for catching the ultrafiltrate. The fluid to be ultrafiltered is introduced into receptacle *F* by means of a pipette fitted with an about 3-mm. wide rubber tubing. The apparatus is screwed on by means of the screw cap (s) and tightened with a small wrench. Air is pumped into the apparatus until the gauge registers the desired pressure which is expressed in pounds.

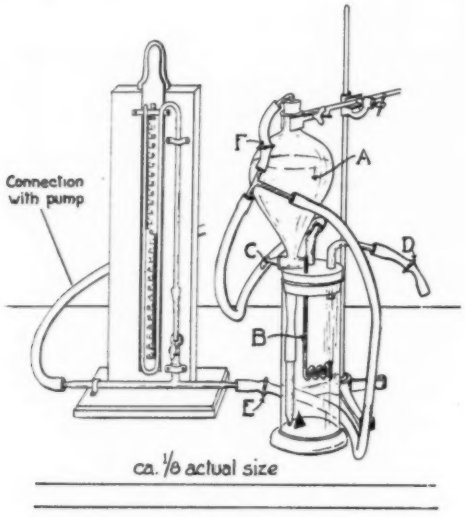


Fig. 3.

COATING OF THE FILTER DISCS

Two kinds of apparatus were used in coating the filter discs.* The apparatus shown in Fig. 3 can be employed when but one or two filter discs are needed for ultrafiltration, whereas the apparatus represented by Fig. 4 permits the coating of nine filter discs at a time.

DESCRIPTION OF APPARATUS SHOWN IN FIGURE 3

The apparatus consists of a suction pump, a manometer, a glass cylinder fitted with a four-hole stopper, and a separatory funnel with a one-hole rubber stopper. The funnel is filled with the collodion solution† and the filter disc is sewed to the glass rod by means of cotton thread. The screw-cock at *D* is tightened while the screw-cocks at *E* and *F* are loosened. Then the apparatus is evacuated. When it is air free the pinch-cock *F* is closed and the

*The filter discs are cut from strong Japanese filter paper.

†Anthony's negative cotton, dried on an electric plate at 80° is dissolved in glacial acetic acid, that contains 2-1½ per cent sodium carbonate.

stop-cock *C* is slightly opened to permit a slow flow of the collodion solution into the cylinder. When the filter disc is completely submerged in the solution stopcock *C* is closed again. Suction is continued until there cannot be seen any air bubbles in the solution. Then the cylinder and the suction pump are disconnected (screwcock *E* is closed). The screwcock *D* and stop-cock *C* are opened. Air thus admitted drives the solution from the cylinder back into the separatory funnel. The rubber stopper carrying the rod with

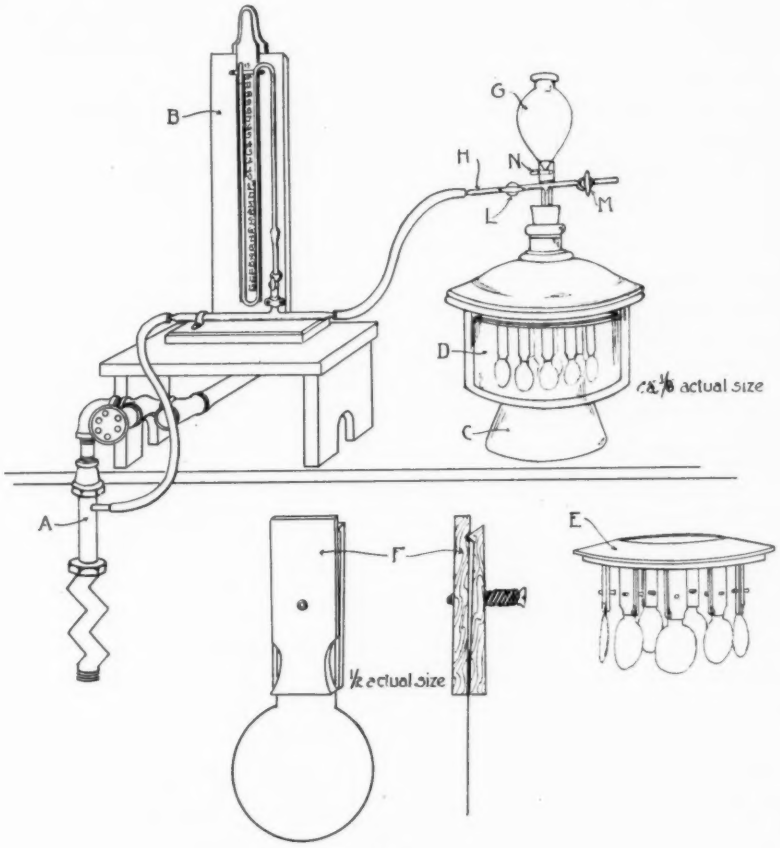


Fig. 4.

the filter disc is lifted out of the cylinder. Ten seconds are allowed between two drops of the excess solution on the disc before the disc is submerged in running water. The filter disc is kept in running water for two days. It is then preserved in distilled water with a drop of chloroform until further use.

DESCRIPTION OF APPARATUS SHOWN IN FIGURE 4

The apparatus consists of a strong suction pump (*A*), a manometer (*B*), a dessicator (*C*), into which a glass jar (*D*) is fitted. This glass jar carried a wooden ring (*E*) to which nine clamps (*F*) are glued. The clamps are made of two strips of wood held together by a simple spiral-shaped spring. The

rubber stopper carries a funnel (*G*). A U tube (*H*) with two stopcocks connects the apparatus with the manometer on one side and with the air supply on the other side.

After the apparatus has been evacuated (stopcock *L* open, stopcocks *M* and *N* closed) part of the solution is admitted into the desiccator through the stopcock *N*. When the manometer again registers evacuation more fluid is admitted, and so on until the filter discs are completely covered. Care must be taken that the collodion solution does not reach the spiral-shaped springs. When the solution is free from air bubbles the suction is discontinued and air is admitted through stopcock *M*. For the completion of the experiment see the above directions.

Before entering into a discussion of the ultrafiltration of blood serum a short description of Lange's colloidal gold test may be in place. The reading of the colloidal gold test depends on various color changes in the tubes of different dilutions.

With normal spinal fluid there is no change of the red color in any of the ten tubes.

In pathologic fluids there may be color changes ranging from a bluish tinge to a red, to complete decolorization, and these changes have been designated by numbers, the unchanged color being designated as zero and complete precipitation by No. 5, the intermediary colors being the numbers between zero and 5.

The clinical application of the colloidal gold test depends on varying degrees of reaction, according to the dilution of the spinal fluid. In general, three types of reaction are found:

1. Those in which the color changes, which depend on the precipitation of the colloidal gold, occur in the first type. This type of reaction has been given the name paretic curve and such a curve would mean 5, 5, 5, 5, 4, 2, 1, 0, 0, 0.

2. Type of curve is one occurring in the middle tubes or in the second zone, giving the curve such as 0, 0, 0, 1, 3, 4, 3, 2, 0, 0. This type of curve is quickly found in tabes dorsalis.

3. Type of curve is known as the meningitic curve and is found in those cases where the precipitation occurs in the tubes of highest dilution or in the third zone. Type of meningitic curve would be 0, 0, 0, 0, 1, 4, 5, 5, 4, 1.

The curves occurring in zones 1, 2, and 3, are not specific for paresis, cerebrospinal syphilis or meningitis. Rare other diseases of the central nervous system may give similar curves.

ULTRAFILTRATION OF NORMAL BLOOD SERUM

The blood was collected in a thoroughly cleansed test tube, allowed to stand in the ice box for not more than half an hour and then centrifuged for 15 minutes. Of the separated serum 3 c.c. were used for the experiments and the globulin test and colloidal gold curve carried out in the second c.c. of the ultrafiltrate, the first c.c. of the ultrafiltrate being discarded. Filter discs coated with 3.5 per cent, 4.0 per cent and 4.5 per cent collodion solution were employed. The results are given in Table I.

TABLE I.

CONC. OF COATING	GLOBULIN TEST	COLLOIDAL GOLD CURVE
3.5 per cent	Negative	0002100000
4. " "	"	0121100000
4. " "	"	0112200000
4. " "	"	0002000000
4. " "	"	1112311000
4. " "	"	311000000
4.5 " "	Trace	0000132200
4.5 " "	Trace	0000131100*
4.5 " "	Negative	3333221000*

*Hemolyzed serum.

In all cases the nitric acid test was strongly positive, and in all but two cases the ammonium sulphate test (globulin test) negative. All ultrafiltrates gave a weak reduction of the colloidal gold solution. To show that the colloidal gold curve in the ultrafiltrate is rather independent of the colloidal gold curve in the blood serum the following two cases may be cited:

	SERUM	ULTRAFILTRATE 4 PER CENT
Colloidal gold curve	5555555554	1112311000
	0004555555	3110000000

All ultrafiltration even of hemolyzed serum yielded colorless ultrafiltrates. Ultrafiltration of normal blood serum shows the presence of a substance that reduces colloidal gold solution.

ULTRAFILTRATION OF SYPHILITIC CEREBROSPINAL FLUID

Spinal fluids were ultrafiltered through discs coated with 3.5 per cent, 4.0 per cent, 4.5 per cent collodion solution. Ultrafiltrates of normal spinal fluids gave no colloidal gold curve. The reduction of colloidal gold solution by ultrafiltrates from syphilitic spinal fluids seems to depend on the quantity of substance present in the spinal fluid reducing the colloidal gold solution. If for instance spinal fluid yielding a weak reduction curve was ultrafiltered the colloidal gold curve of the ultrafiltrate was practically negative. If on the other hand spinal fluid that gave a very strong colloidal gold curve was ultrafiltered the filtrate exhibited a positive colloidal gold curve. This was best shown in the following case:

CONC. OF COATING	SPINAL FLUID	ULTRAFILTRATE
3.5 per cent	55553321000	5554110000

GENERAL REACTIONS IN ULTRAFILTRATES

Sera with positive Wassermann reactions were ultrafiltered through paper coated with 4.0 and 3.5 per cent collodion glacial acetic acid solution. The results are tabulated in Table II.

Of the two sera ultrafiltered through 4 per cent coating both had a definite colloidal gold curve and positive globulin tests. The same sera when ultrafiltered through 3.5 per cent coating gave no colloidal gold curve. Only one serum ultrafiltered through 3.5 per cent coating gave a colloidal gold curve.

TABLE II

	SERUM			U SERUM 4%			U SERUM 3-½%			REMARKS
NUMBER	W.	C.G.	GL.	W.	C.G.	GL.	W.	C.G.	GL.	
0861	4 pos.	3?s3		?	w3	2 pos.	1 pos.	neg.	?	control to U3-½ ant.
115764B	4 pos.	s1s2s3		neg.	w2w3	2 pos.	?	neg.		
115055J	4 pos.	neg.					neg.	w3		
2255R	1 pos.	w2w3	2 pos.				w3	neg.		
17686R	?	s1s2	2 pos.		w2			neg.		
17749D	?	neg.			w1w2	?	w2w3	trace		
17686	neg.	neg.	4 pos.	neg.	neg.	½ pos.	neg.	neg.	neg.	
175770	neg.			neg.			neg.			
H	neg.	w3	2 pos.					neg.	2 pos.	

Keys
W = Wassermann reaction.
c. g. = colloidal gold test.
U serum = Ultrafiltrate of serum
U serum 4% = serum ultrafiltered through filter paper coated with 4% collodion acetic acid solution.
U serum 3½% = serum ultrafiltered through paper coated with 3½% collodion acetic acid solution.
s2s3 = strong reduction in tubes 456, and tubes 789.
w2w3 = weak reduction in tubes 456, and tubes 789.
4 pos. = four-plus signs.

Of two bloods with a questionable Wassermann one gave a colloidal curve in the serum ultrafiltered through filter paper coated with a 4 per cent solution and the other ultrafiltered through a disc coated with a 3.5 per cent solution.

Ultrafiltration of nonluetic bloods (negative Wassermann) was run as controls. The ultrafiltrate did not give a colloidal gold curve; two of them, however, had a positive globulin test.

CONCLUSIONS

1. The ammonium sulphate test (globulin test) is negative in the majority of ultrafiltrates of normal blood serum.

2. The ultrafiltrates of nonsyphilitic blood sera give a reduction of the colloidal gold solution in almost all cases. The same is true of the ultrafiltrates of syphilitic sera.

3. The ultrafiltrates of normal cerebrospinal fluid give no colloidal gold curve.

4. The reduction of colloidal gold solution by ultrafiltrates from syphilitic spinal fluids seems to vary with the quantity of the substance reducing the colloidal gold solution present in the original spinal fluid.

5. The substance giving the Wassermann reaction in syphilitic blood does not seem to be ultrafiltrable.

NOTE: I wish to express my appreciation to Mr. Victor Rochrich, St. Paul, for making the ultrafiltration apparatus, to Dr. Margaret Warwick for the determinations of the colloidal gold tests, and to Dr. H. T. Ogden for the determination of the Wassermann reaction.

METHOD AND DIAGNOSTIC VALUE OF QUANTITATIVE DETERMINATION OF SUGAR IN THE CEREBROSPINAL FLUID*

By Guy H. Moates, M.D., and J. Jay Keegan, M.D., Omaha, Nebr.

THE quantitative determination of sugar in the cerebrospinal fluid has been a rather recent development in laboratory diagnosis.[3] It has received special attention in relation to epidemic encephalitis in which it has been claimed by several, Thalimer and Updegraff,[4] Foster,[5] Netter, Bloch, and Dekemwer,[6] Kraus and Pardee[7] and Coope,[8] to be fairly constantly increased.

Several methods have been advocated in the last two or three years and apparently the most accurate results have been obtained by some modification of the technic used by Lewis and Benedict[2] for the quantitative determination of sugar in small amounts of blood. The method used in this series is a modification of this technic using 4.0 c.c. of cerebrospinal fluid instead of blood. This method seems to have the advantage over any other because there is a standard color which is prepared from a solution with a known glucose content and also one is comparing shades of red and yellow which can be matched with a lesser degree of error than the blue of copper sulphate solutions.

The rapid methylene blue method advocated by Yasharia and Hattori[1] was used to compare some of the readings in this work, but it was abandoned as a routine measure because it was so unreliable and no accurate idea of the amount of sugar present could be obtained.

There has been considerable discussion as to the percentage where the sugar content of the cerebrospinal fluid is to be considered pathological or if it has any diagnostic value. Two hundred three specimens were examined in this series. No attempt was made to select them from any particular group of patients, but they were taken from specimens that were sent to the laboratory for routine examination.

CEREBROSPINAL SUGAR

Table I shows that the average sugar content for the 203 specimens was 0.0585 per cent. The highest reading was obtained in a severe case of epidemic encephalitis, being 0.288 per cent, and the lowest reading was in a case of tuberculous meningitis, being 0.013 per cent. The highest average for any series of cases was in the group of epidemic encephalitis, being 0.081 per cent, and the lowest readings were obtained in the group of meningitis of infectous character. These findings are practically in accordance with those of Thalimer and Updegraff;[4] Foster;[5] Netter, Bloch, and Dekemwer;[6] Kraus and Pardee;[7] and Coope.[8]

*From the Department of Pathology, University of Nebraska, College of Medicine, Omaha.

A series of experiments were performed on a large dog to determine the effects of various substances on the sugar content of the cerebrospinal fluid obtained by cisternal puncture. A normal fluid was first obtained and found to contain 0.086 per cent sugar. Two-tenths of a cubic centimeter of turpentine in one cubic centimeter of physiological sodium chloride was injected into the cisternal space. There was a definite increase in the cell count to 105 per cubic millimeter and a slight increase in the sugar content to 0.092

TABLE I

SHOWING THE AVERAGE, THE HIGHEST AND THE LOWEST, PERCENTAGE READINGS OF THE SUGAR CONTENT OF THE CEREBROSPINAL FLUID IN DIFFERENT DISEASES

CLINICAL DIAGNOSIS	NUMBER	AVERAGE %	HIGH %	LOW %
Tabes dorsalis	35	0.055	0.075	0.031
Syphilis, not of the central nervous system	33	0.054	0.101	0.041
Paresis	32	0.059	0.090	0.045
Epidemic encephalitis	29	0.081	0.288	0.046
Tabeo-paresis	8	0.054	0 069	0.046
Dementia praecox	6	0 047	0.054	0.040
Syphilitic optic atrophy	6	0.053	0.070	0.038
Toxic psychoses	5	0.055	0.065	0.051
Vascular C-S spyhilis	5	0.063	0.085	0.046
Psycho-neuroses	4	0.055	0.065	0.040
Tubereulous meningitis	4	0.0175	0.021	0.013
Alcoholic psychoses	4	0.050	0.063	0.041
Arteriosclerosis dementia	4	0.058	0.060	0.056
Syphilitic meningitis	3	0.063	0.120	0.031
Paralysis agitans	3	0.076	0.088	0.066
Typhoid meningitis	3	0.030	0.032	0.028
Nephritis	2	0.049	0.055	0.042
Manic-depressive psychoses	2	0.062	0.062	0.062
Epilepsy	2	0.065	0.065	0.065
Meningococcus meningitis	2	0.020	0.032	0.018
Alcoholic meningismus	1	0.107	0.107	0.107
Toxic meningismus	1	0.096	0.096	0.096
Miliary tubereulosis	1	0.062	0.062	0.062
Brain tumor	1	0.042	0.042	0.042
Spinal cord tumor	1	0.050	0.050	0.050
Cerebellar hemorrhage	1	0.117	0.117	0.117
Post traumatic syndrome	1	0.091	0.091	0.091
Pneumococcus meningitis	1	0.025	0.025	0.025
Sinusitis	1	0.048	0.048	0.048
Normal individual	1	0.050	0.050	0.050
Total	203	0.0585	.....	.....

per cent in the fluid which was withdrawn 48 hours later. The dog was allowed to rest for 6 days and another puncture was performed and normal fluid obtained. At this time 2 drops of Dakin's hypochlorite solution were injected with a resultant immediate severe reaction. Fluid was obtained the next day and showed a cell count of 4,150, increased protein, but a normal sugar content, 0.083 per cent. Fluid was obtained on each of the three following days with no significant difference in the sugar content and with a steady decrease in the cell count and the protein. After the fluid had become normal, the dog was placed under ether anesthesia and fluid was obtained. This showed a normal cell count and protein, but a slight increase in the sugar content, 0.098 per cent. This increase might be attributed to the stimulating effect of ether anesthesia on the secretion of the choroid plexus.[14]

DISCUSSION

An analysis of the 203 specimens studied shows a definite increase in the sugar content in most of the cases associated with a cerebral irritation. The other cases are within the limits which were noted by Foster[5] as being a normal sugar content of the cerebrospinal fluid. These findings disagree with those of Stevenson[9] who found no significant increase of sugar in the cases of epidemic encephalitis and a greater variation in the cases of neurosyphilis.

Several authors have attempted to show some connection between the colloidal gold curve, the cerebrospinal fluid Wassermann, the cell count, the protein and the sugar content. In this series there is no evident relationship between the sugar content and any of the other serological findings. No case of epidemic encephalitis showed a typical paretic curve as reported by Howell,[10] there being no characteristic colloidal gold curve observed.

The cause of hyperglycorrhachia is as yet an unsolved problem. Kahler[11] thinks it is caused by most stimulations and inflammations of the brain. Hypoglycorrhachia in the cases of meningitis is probably due to the reducing action of the invading microorganism and not due to the inflammation they cause. Specimens of cerebrospinal fluid which were collected under sterile precautions and kept in the ice box (8° C.) did not vary any appreciable amount in sugar content and could be used for quantitative determinations 96 hours after having been withdrawn. These same specimens when inoculated with the pneumococcus, certain strains of the streptococci, the meningococcus or the tubercle Bacillus and kept at ice box temperature 24 hours showed a constant decrease in the sugar content.

It has been shown fairly definitely by several investigators[15] that certain strains of the pleomorphic streptococci have no reducing powers. Such a microorganism producing inflammation of the brain, as is suspected in epidemic encephalitis, might be the cause of hyperglycorrhachia. This would be an additional point in favor of Bonhoeffer's[12] claim that encephalitis is due to a pleomorphic streptococcus. Hassin[13] states that epidemic encephalitis is an inflammation and not a degenerative process and this statement agrees with that of Kahler[11] and that the hyperglycorrhachia is due to inflammation and overstimulation. This may explain the high sugar content in the cases of alcoholic and toxic meningismus of this series.

Thalmer and Updegraff[4] think the high sugar content of the cerebrospinal fluid is due to a change in the blood sugar, but this does not seem possible as none of the cases of encephalitis of this series showed a glycosuria or a glycemia.

Kahler[11] gives three tentative explanations of the hyperglycorrhachia: (a) abnormal permeability of the choroid plexus for sugar, based on Blumethal's work showing that the cerebrospinal fluid is formed by transudation and secretion; (b) abnormal secretion of glucose in the plexus cells based in the findings of Yoshimura who demonstrated glycogen in these cells and (c) abnormal metabolic process in the brain substance. The last two are the most commonly accepted at present.

CONCLUSIONS

1. The normal range of the cerebrospinal sugar is between 0.040 per cent and 0.068 per cent.

2. Sugar content of the cerebrospinal fluid is distinctly increased in most cases of epidemic encephalitis and has a diagnostic significance.

3. Sugar content of the cerebrospinal fluid is decreased in infectious meningitis probably due to the reducing powers of the invading micro-organisms.

4. There is no apparent relation between the sugar content of the cerebrospinal fluid and the Wassermann reaction, colloidal gold curve, cell count, globulin or total protein.

BIBLIOGRAPHY

[1]Yasaharia, Michio, and Hattori, Shunjiro: Am. Jour. Dis. Child., 1921, xxii, 218.
[2]Lewis, Robert C., and Benedict, Stanley R.: Jour. Biol. Chem., 1915, xx, 61.
[3]Schaffer, Oscar M., and Schrader, Louis C.: Am. Jour. Dis. Child. xi-1-'16.
[4]Thalimer, William, and Updegraff, Helen: Arch. Neuro. and Psych., 1922, viii, 15.
[5]Foster, Harold E.: Jour. Am. Med. Assn., 1921, lxxvi, 300.
[6]Netter, Arnold, Bloch, Sigismoid, and Dekeuwer: Compt. rend. Soc. de Biol., Paris, 1920, lxxxiii, 338.
[7]Kraus, Walter M., and Pardee, Irving H.: Arch. Neuro. and Psych., 1921, v, 710.
[8]Coope, R.: Quart. Jour. Med., 1921-1922, xv, 1.
[9]Stevenson, Lewis D.: Arch. Neuro. and Psych., 1921, vi, 292.
[10]Howell, Katherine M.: The Colloidal Gold Curve in Epidemic Encephalitis, Arch. Neuro. and Psych., 1922, vii, 229.
[11]Kahler, H.: Changes in the Sugar Content of the Cerebrospinal Fluid in Internal Disease and Nervous Affections, Wein. klin. Wehnschr., 1921, xxxv, 8.
[12]Bonhoeffer, K.: Epidemic Encephalitis, Deutsch. Med. Wehnschr., 1921, xlvii, 229.
[13]Hassin, G. B.: Histopathologic Findings in Case of Superior and Inferior Polioencephalitis with Remarks on the Cerebrospinal Fluid, Arch. Neuro and Psych., 1921, v, 552.
[14]Pettit, A., and Girard, J.: The secretory processes in the lining cells of the choroid plexus of the lateral ventricles following administration of muscarine and ether, Compt. rend. Soc. de Biol., Paris, 1901, liii, 825.
[15]Rosenow, E. C.: Experimental Studies on the Etiology of Epidemic Encephalitis, Jour. Am. Med. Assn., 1922, lxxix, 443.

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EDITORIALS

Sodium Chlorid Restriction in Hypertension

THE treatment of hypertension with diets of low salt content is not new. Such dietary measures have been studied in the past chiefly by various French observers. In this country, as a rule, salt restriction has not been pushed to an extreme, and only occasional investigators have insisted upon a chlorid intake of less than two grams per day. Opinions of the efficacy of rigid salt restriction have been distinctly at variance. This appears due, in part at least, to the fact that salt restriction has not often been enforced rigidly enough to produce the desired results. Allen and Sherrill, who have given much time to a study of this method, find that best results are obtained with a chlorid intake sufficiently reduced that no more than one-half gram of sodium chlorid is excreted in the twenty-four hour urine. Since this rigid restriction occasionally causes deficiency symptoms, they insist that no clinician who has used salt restriction with unsatisfactory results, has used it properly unless he has observed salt deficiency symptoms.

The Morristown investigators have worked on the hypothesis that hypertension, particularly uncomplicated hypertension, is a disease resulting from

error in salt metabolism, and that individuals with such symptoms are unable to tolerate normal quantities of sodium chlorid. Their results tend to substantiate this claim. As yet they make no suggestion as to the underlying cause for the error in salt metabolism.

Normal blood pressure was restored in 18.9 per cent of 180 severe cases, therapeutic success without complete restoration of normal pressure was obtained in 41.9 per cent, and transitory benefit followed by relapse or death occurred in 8.9 per cent. Complete failure was encountered in 30.5 per cent. Treatment lasted over periods from one month to one year. The entire group was divided into four classes. Those with pure hypertension and high plasma chlorid values, those with uncomplicated hypertension and high plasma chlorid values, those with uncomplicated hypertension and relatively low blood chlorids, cases with associated nephritis, and those with diabetes. Best results were observed in the first group. A suggested explanation of less successful results in the second group is that in the first the hypertension was more purely functional and associated with the high chlorid readings, while in the second the increased pressure followed more permanent organic changes. Poorest results were observed in those cases associated with nephritis. Complicating diabetes, when properly treated, in no way interfered with satisfactory results from salt restriction. Although uncomplicated cases were classified according to high and low plasma chlorid content, the authors found no constant correlation in their series between the chlorid level and the degree of hypertension. The authors devote little attention to a classification of their cases according to the degree of arteriosclerosis present. We hope that this phase will receive further study.

Allen and Sherrill found no such close association between obesity and hypertension as was formerly assumed to hold. The majority of patients had normal or slightly subnormal body weights. Improvement occurred independently of the presence or absence of abnormal weight, except when increased weight was due to fluid retention with or without recognizable edema. They found that a normal blood urea nitrogen concentration on a liberal protein diet is probably as conclusive indication of adequate nitrogen excretion as any other single test. Retention of urea or nonprotein nitrogen was found to bear no relationship whatever to the degree of hypertension. In those cases with impaired renal function and nitrogenous retention, protein intake was restricted along with salt intake, but with normal nitrogenous metabolism the protein intake was not reduced at all. In some of the more severe nephritics it was found necessary to first treat the nephritis with a low protein diet and later to reduce the salt intake. Otherwise alarming uremic symptoms occasionally developed. The latter were quickly relieved by the giving of ten grams of sodium chlorid daily. Albuminuria and cylindruria were usually uninfluenced by salt restriction. The minority of cases showed unmistakable diminution thereof.

Increased plasma sugar values have recently been described in essential hypertension and improvement in symptoms has been ascribed to reduction of carbohydrate intake. Allen and Sherrill found the blood sugar values

normal in a higher percentage of group I cases than in the second group with low plasma chlorid levels. In the third group, associated with nephritis, the plasma sugar was still more constantly elevated. It is suggested that the increased sugar values occur at a later stage of the disease, when permanent organic changes have occurred and may be due to arteriosclerotic changes in the pancreas.

In cases successfully treated there was a fall not only of the systolic but also of the diastolic blood pressure. The latter was distinctly more stubborn and was reduced to a less extent than the former. It is a matter of general observation that hypertension cases in which the blood pressure has been reduced to too great an extent are subjectively and often objectively much more seriously affected than when the pressure was higher. For this reason certain authors have assumed that the development of hypertension is primarily a compensatory affair and attempts should not be made to alter it to too great a degree. When the blood pressure has fallen with resulting unpleasant symptoms, it is usually found that the systolic pressure has been decreased out of proportion to the diastolic reduction and that the pulse pressure has thereby become unusually small. It appears probable that the unpleasant symptoms have been due to the resulting small pulse pressure, with correspondingly reduced functional capacity of the cardiovascular apparatus. If strict salt restriction will reduce the diastolic pressure proportionately or nearly proportionately to the systolic reduction, we will be in a position to understand and to expect good clinical results from the method advocated by Allen and Sherrill.

The results in cases treated by Allen and Sherrill were obtained after treatment varying from a few days to as long as one year. This indicates the necessity of perseverance in the diet even though immediate improvement is not observed. Those cases responding promptly with fall in blood pressure are of better prognosis than those in which the blood pressure is reduced only after a longer period. The diet was regarded as "salt-free" when the sodium chlorid content of the urine was kept at or below 0.5 gm. per day. Most of the individuals remained on such a diet continuously. Occasionally privation symptoms occurred with weakness, anorexia, vertigo, etc., necessitating an increase in the salt intake. A careful balance must finally be attained, the patient being given a sufficiently low salt intake that he may show no salt retention symptoms and yet sufficiently high that privation symptoms do not supervene. Since the levels at which both groups of symptoms appear vary in individual cases, this sometimes requires patient standardization. The most difficult cases are those in which the pressure is only slightly reduced by a chlorid restriction which causes privation symptoms. The best clinical diet in these hopeless cases is afforded by a chlorid allowance which gives a mixture of mild privation symptoms and mitigated hypertension symptoms.

Chlorid restriction was found to act favorably on the serious accompaniments of hypertension, such as cardiac failure, incipient pulmonary edema, retinitis and vascular crises, including to some extent angina pectoris.

The authors emphasize that their work has been done on a series of severe cases and that the probability of improvement would be correspondingly greater in a series with mild or early hypertension. No attempt is made to explain the presence of an abnormal salt metabolism predisposing to hypertension. It is the experience of most of us that individuals with hypertension are unusually heavy salt eaters and it may be that the disease may arise in part from chronic overload.

The actual limitations of our knowledge of the etiology of hypertension are evidenced by the multiplicity of therapeutic procedures. The majority, such as hydrotherapy, bleeding, vasodilation, rest, etc., are purely symptomatic. It has long been supposed that hypertension is in some way related to error in protein metabolism, and protein restriction has therefore been the most generally accepted treatment. Just as typhoid fever and the paratyphoids were formerly classed under the general diagnosis of typhus fever, so hypertension was formerly associated exclusively with chronic nephritis and considered to be an event of the later stages of Bright's disease. With the recognition of essential hypertension as a distinct disease which may occur with minimal renal lesions a distinct diagnostic advance was made, but the treatment has continued to be based upon the older concept of protein restriction in renal disease. We can scarcely yet state that an error in protein metabolism is not the cause of essential hypertension. It does appear, however, that nitrogenous metabolism varies around normal limits in this disease and that the feeding of relatively high protein diets in no way interfered with good results from salt restriction. Most experimental work with high protein diets has been directed to the production of arteriosclerosis rather than hypertension. Thus Newburgh has recently produced arteriosclerosis strictly by high protein feeding. However, the production of such a condition experimentally in an herbivorous animal is quite dissimilar to the same procedure in man.

Strause and Kelman fed hypertensive individuals with and without associated nephritis, varying daily protein intakes. They could discover no relationship between the protein intake and the blood pressure. Nitrogen retention was influenced by changes in nitrogen intake but the blood pressure could not be so influenced. Squier and Newburgh, after feeding patients with hypertension amounts of protein well over 150 gms. per day, concluded that high protein diets over a short period have no effect on the blood pressure.

The occurrence of hyperglycemia in hypertension, emphasized especially by Herrick, may be explained merely as a secondary phenomenon resulting from organic changes in the pancreas, or, in cases associated with nephritis, as analogous to the nitrogenous retention.

It should be noted that the findings of Allen and Sherrill with regard to hyperglycemia are somewhat at variance with those recorded by Härle. Whereas the former found the plasma sugar value most constantly elevated in hypertensive cases with nephritis, Härle found the reverse to be the case. In one-half of cases with kidney lesions and hypertension the blood sugar was

on the upper border of the normal range. Frank hyperglycemia was rarely observed. On the other hand, in cases without demonstrable renal lesions, a definite hyperglycemia was seen in one-fourth and an upper normal range in another one-fourth. Botti found blood sugar increased and sugar tolerance diminished in the presence of hypertension, especially when associated with arteriosclerosis.

Following the work of Cannon, many have suggested that hypertension results from an increased adrenalin discharge in the system. Hülse was unable to demonstrate increased adrenalin concentration in the arterial or venous blood of hypertensive individuals, even though his frog preparation was sensitive to concentrations of adrenalin of one to one billion.

Orr and Innes, working on the hypothesis that pressor substances are derived from protein split products, regulated the fluid intake of their patients, and found that with increased fluid consumption the blood pressure was somewhat reduced. Their interpretation was that the hypothetical pressor substances were diluted, and perhaps to some extent removed by the increased diuresis. Their variations were not, however, unquestionably beyond the normal range.

Among other therapeutic measures based upon conceptions of the etiology of hypertension we must still number prohibition of nicotine and alcohol, reduction of overweight and removal of focal infection. The purin bases have ceased to incite terror.

One cannot say that it has been shown that hypertension is due to an error in salt metabolism. Nevertheless it is worthy of note that Allen and Sherrill have successfully relieved a fairly large proportion of their severe hypertensive cases by rigid restriction of salt intake without the application of other therapeutic measures.

BIBLIOGRAPHY

Allen and Sherrill: Jour. Metabolic Research, 1922, ii, 429.
Herrick: Virginia Med. Monthly, 1922, l, 163.
Botti: Policlinico, 1922, xxix, 249.
Härle: Ztschr. f. klin Med., 1921, xcii, 124.
Hülse: Ztschr. f. im. Med., 1922, xliii, 1.
Orr and Innes: Brit. Jour. Exper. Path., 1922, iii, 61.

—*W. T. V.*

At Last, the Bed Bug

THIS occasional intruder has until now held a position of inferior importance among percutaneous feeders in that it has been considered to be nosetiologically innocuous. L. H. Dunn, entomologist at the Board of Health Laboratory, Ancon, Canal Zone, in 1921, conducted several experiments to determine any relationship between the tropical bed bug and the transmission of relapsing fever. Although unable to complete his work before his departure from Panama, Dr. Dunn made several interesting and suggestive observations. He first attempted to transmit the disease through the bite of

the bug. Thus he allowed 49 hungry bugs to bite an individual ill with relapsing fever, and on each of the seven succeeding days each bug fed upon a single white rat. During this period the rat received 704 bites. He did not develop relapsing fever. In the same way bugs were fed on infected rats and later were allowed to bite monkeys. The monkeys did not develop relapsing fever. It was demonstrated, however, that at the time of feeding on the monkeys the bugs were carrying spirochetes in the intestinal contents and in the salivary glands.

Positive results were obtained by mouse inoculation with suspensions of macerated bugs which had been allowed to feed on infected animals as long as thirty days previously. On dissection, bugs were found to be infected with spirochetes two days, eight days and fifteen days after feeding on infected animals. The microorganisms were present in the gut contents and salivary glands two days after feeding but were absent from these localities eight and fifteen days after. At these two later intervals spirilla were found in the coelomic fluid. Not all bugs were infected.

Although bed bugs did not experimentally transmit relapsing fever the observation that they are infected for appreciable periods after feeding on hosts sick with the disease is of considerable interest. The fact that relapsing fever was caused by the injection of macerated specimens of such bugs calls for further work along this line. More detailed control studies will be necessary. It is unfortunate that the author was unable to complete his studies before leaving the canal zone.

—*W. T. V.*

*Dunn: Am. J. Trop. Med., 1923, iii, 345.

BOOK REVIEWS

(Books for Review should be sent to Dr. Warren T. Vaughan, 404 Professional Building, Richmond, Va.)

*The Urethra and the Urethroscope**

THE author's experience has eminently fitted him to conceive and write this small handbook. He describes the anatomy and surface appearance of the normal male and female urethra as seen through the urethroscope, together with the appearance in various pathological conditions. He discusses the comparative virtues of different types of urethroscopes and outlines the accepted methods of treatment without discussing in detail moot therapeutic considerations. Though condensed, the book is quite thorough and should be highly useful to those doing urethroscopic work. It is well illustrated.

Practical Dietetics†

WITH the rapidly changing and developing concepts of dietary treatment in various diseases it is indeed a task to keep a reference book on dietetics strictly up to date. One must incorporate the newer methods which are rapidly displacing older empiric formulae; one must discriminate between recent suggestions of undoubted worth and the much more numerous unscientific dietaries still appearing in current literature; and one must use great discretion in eliminating from former editions those methods which are distinctly obsolete or inferior.

All of this the author has accomplished. While some diets now little used are retained chiefly for their historical interest, the book as a whole is thoroughly up to date. Written primarily for nurses and dietitians it should find a place on the desk of all physicians attempting to practice dietotherapy in conjunction with other medical treatment.

The first half of the book is devoted to a consideration of foods and their preparation with special emphasis placed on those foods and delicacies which are found chiefly in the sick room. The second half deals with diets used in special diseases, such as typhoid fever, diabetes, gout, obesity, deficiency dis-

*The Urethra and the Urethroscope: A Manual of Practical Urethroscopy. By F. Carminow Doble, M.R.C.S., L.R.C.P., London. Temporary Captain R. A. M. C. Officer in Charge Gonorrheal Division, Military Hospital, London. With foreword by Major A. F. Frost, O.B.E.R.A.M.C. Officer Commanding Military Hospital, Rochester Row. Pp. 120. Cloth. Henry Frowde & Hodder & Stoughton, London, 1923.

†Practical Dietetics. Diet in Health and Disease. By Alida Frances Pattee. Graduate, Department of Household Arts, State Normal School, Framingham, Mass. Former Instructor in Dietetics, Bellevue Training School for Nurses, Bellevue Hospital, New York City. Former Instructor at Mount Sinai, Hahnemann, and the Flower Hospital, Training Schools for Nurses, New York City; Lakeside, St. Mary's Trinity, and Wisconsin Training Schools for Nurses, Milwaukee, Wis.; St. Joseph's Hospital, Chicago, Ill., St. Vincent de Paul Hospital, Brockville, Ontario, Canada. Fourteenth edition. Completely revised. Cloth. Pp. 687. Price $2.60. A. F. Pattee, Publisher, Mount Vernon, New York, 1923.

eases, ulcer, nephritis, anemia, etc. The chapter devoted to postoperative diets, infant feeding and the feeding of young children should be found to be particularly useful.

The Spectroscope

THE first edition of this book came out in 1907 and many changes have been made to bring this second edition up to date. It is still a book of modest size (about 200 pages) that is intended to help the man who actually uses a spectroscope.

After a chapter on the refraction of light and on the formation of spectra the author describes the various forms of spectroscopes, their adjustment and their operation. He also adds two chapters on spectrophotography.

The difficult problem in a book of this size is to decide what to leave out. For example, he has about one page on Bioluminescence (the emission of light by living organisms) and it is doubtful if he can give enough in such a small space to make it worth while. On page 180 he refers to Planck's quantum and to Bohr's atom and here again it is doubtful if he gives enough to make such highly technical and theoretical subjects intelligible. In this connection he makes the statement, "Bohr concludes that when an electron is thrown out from one stationary motion to another it radiates out abruptly the difference of energies represented by the change in orbit. Now, apart from the difficulty of the expression "stationary motion" it is generally assumed that when the electron is "thrown out" from a stable orbit to one less stable it absorbs energy and then radiates energy when it falls back to the more stable orbit.

Typographical errors are as difficult to keep out as are flies from a well regulated home and are quite as annoying to the author. On page 103 is the statement, "Over thirty years ago Rowland photographed the solar spectrum up to 7300 A.U." This is evidently a hang-over from the first edition which failed to get revised. On page 170 is found 10^{-18} instead of 10^{-8} thus making the x-rays ten thousand million times too short.

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*The Spectroscope. By T. Thorne Baker, A. M. I. E. E., F. R. P. S. Author of "Radiographic Technique." Cloth. Price $3.00. Second edition. Pp. 208. William Wood & Company, New York, 1923.

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Footnotes.—Where an author wishes to use footnotes at bottom of each page instead of the bibliography at end of article, the footnotes should be written in the text, but separated from it by horizontal lines above and below, or *better,* place them at bottom of each page. Use figures to indicate these footnotes, and number consecutively (1, 2, 3, etc.) throughout the article. If in addition to the bibliography mentioned above it is desired to use footnotes on certain pages, these can be indicated by an asterisk (*).

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References. (Read these.)

[1]Billings, J. S.: Our Medical Literature, Trans. VII Intern. Med. Congress, Lond., 1881, i, 54-70.

[2]Mayer, Emil: Medical Literature and its Preparation, Med. Record, N. Y., 1915, lxxxvii, 1019-1021.

Allbutt, T. C.: Notes on the Composition of Scientific Papers. London, Macmillan, 1904.

McCrae, Thomas: The Use of Words, Jour. A. M. A., Chic., 1915, lxv, 135-139.

[3]Suggestions to Medical Authors, issued by the A. M. A. Press, Chic., A. M. A., [1914 (?)].

[4]Place, F.: Bibliographic Style in Medical Literature, Med. Record, N. Y., 1913, lxxxiii, 157-160.